Henry Ford Hospital Medical Bulletin

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THE HENRY FORD HOSPITAL MEDICAL ASSOCIATION

DWIGHT C. ENSIGN, M.D.*

Again we are privileged to publish in this issue of the "Bulletin", some of the papers presented by former staff members at the fourth meeting of the Henry Ford Hospital Medical Association. The committee charged with the selection of essays to be published regrets that limitation of space prevented the inclusion in this issue of several of the really valuable papers which were read at this meeting. It was the feeling of most of those in attendance that the scientific program was of unusually high caliber throughout.

This fourth in the series of meetings of the Henry Ford Hospital Medical Association was held at the Hospital on Friday and Saturday, May thirty-first and June first. The general sessions on Friday were held in the auditorium, and the sectional meetings on Saturday were accommodated in the various conference rooms of the Clinic Building.

At the banquet on Friday evening, held at the Hotel Statler, the speaker was Bud Guest of radio station WWJ. Dancing followed the banquet.

Dr. William A. Altemeier gave over his duties as President to Dr. Elston L. Belknap. Dr. A. P. Wilkinson was elected as Vice-President and President-Elect, and Dr. James T. Howell was elected Secretary-Treasurer. Dr. Belknap named to the Administrative Board Drs. C. L. Reyner, Leston S. Whitehead and M. Andrew Sapala, who will serve with the elected officers in making plans for the next meeting of the Association.

It was a matter of regret that the enforced change of date for the last meeting prevented some loyal members from coming this year, due to demands preceding the meeting of the American Medical Association. However, it was a real pleasure to welcome several members who had not attended previous meetings.

*Ex-Secretary-Treasurer, Henry Ford Hospital Medical Association

UNSUSPECTED INDUSTRIAL POISONINGS DISCOVERED IN SMALL INDUSTRIES*

ELSTON L. BELKNAP, M.D.**

The problem of poisoning occurring in large industry is not a new one but is daily becoming more complex with the demands of our heavy chemical industrial life. However, large industries are so well equipped with medical personnel and ancillary services that a real case of occupational disability and death is very rare.

In the small industries, however, which make up more than 80% of employees, the problem of unsuspected poisoning is not rare, contrary to current medical opinion. Also, such cases are not infrequently fatal. To a large extent this is due to the fact that neither the employer nor the employee in the small industry realize the potential dangers of the materials with which they work. Also, it is unusual to find that a doctor or nurse has been asked to come in to look after the health of the worker even on an occasional or part-time basis.

Moreover, small industries have another additional factor in that the process is not too well understood by the manager-owner.

Those who are familiar with this field know that there is an urgent need here for medical supervision and advice. There is also a very real opportunity for the general practitioner and internist who with some intensive study can qualify themselves to be competent consultants to industry as a part-time service. They will not only find it remunerative, but it will give them something of the thrill of the detective who is tracking down a murderer or a potential murderer. Furthermore, when the part-time medical consultant to industry follows a definite plan of attack on the problem, he should be able to prevent disability and death as effectively as his full-time brother physician in the large industries.

Medical students are prone to think that they will have only a millionaire or at least a white-collar clientele, but all practicing physicians know that the majority of their patients work in some industry. It therefore behooves them to ask the simple but often forgotten question, what is your occupation?

The following cases of serious but unsuspected poisoning occurring in groups of workers in small plants illustrate the earnestness with which the employer and the physician must face these problems.

Whenever we consider the possibility of poisoning from toxic dusts, fumes, vapors, or gases in industry, we remember that the commonest portal of entry is by inhalation; the next is by skin absorption; rarest from ingestion by mouth.

One should again remember the point of attack on a specific organ or body system which differs with different toxic materials. In some cases the brain or

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*Presented May 31, 1957 before the Henry Ford Hospital Medical Association, Detroit, Michigan.
**Professor of Occupational and Environmental Medicine, Marquette University Medical School.

central nervous system or even the peripheral nervous system will be involved, while in others it will be the blood-forming organs, the liver, the kidney, or the muscles themselves. Toxic involvement of the lung proper is rare, except by irritation in certain instances, contrasting the effect on the lung and lymphatic structures following the inhalation of certain non-toxic but fibrogenic dusts such as silica.

When one recalls that the circulation time from the lung to the general system is a matter of a few seconds and that the area exposed in the pulmonary alveoli is upwards of 60 to 70 square meters, he can realize how rapidly toxic materials are absorbed by inhalation thus exposing the entire body, system by system.

The doctor's first contact with patient and his family will be the presenting symptoms. Consider first, for example, the headache of carbon monoxide absorption or mild intoxication with characteristic pressure over the temples associated with dizziness and nausea. This is suggestive of the possibility of carbon monoxide poisoning in its preliminary and warning stage. Carbon monoxide exposure, moreover, occurs in the home, in the automobile, as well as at the plant, wherever there is incomplete combustion of carbon.

In any of these places the physician should not be satisfied to treat symptoms only after the disease or poisoning is full-blown. The moment he hears of a new process or suspects a new hazard, he should be eager to become familiar with all the details, both engineering and medical. Only then will he be able to help prevent the occurrence of disability, temporary or permanent. I am thus detailing the currently known facts of my most recent case to emphasize the importance of the physician's responsibility to participate in the control of his patient's working environment.

Within the week I was asked to see a young man supposed to be a malingerer who had developed just this type of headache within the first few hours after he was assigned to work on a new type of welding process. As you realize, welding of steel and its alloys is now an integral part of many modern manufacturing processes. Temperature of the arc, particularly when the hard alloy metals are being welded, often runs from 4000 to 4500 degrees Fahrenheit. Since the war it has been found that welding can be done with many fewer imperfections in the welded area if the flame is shielded by some type of an inert gas to prevent oxygen in the surrounding air from causing imperfections in the weld due to oxide bubbles. At first rare gases such as argon and helium, the so-called Heliarc process, were used as the shielding gas. This appeared harmless except occasionally when in an enclosed space the presence of ozone irritated the lung proper.

Recently it has been found that carbon dioxide is just as effective and much less expensive than the rarer gases. Therefore, you can see that carbon dioxide will soon be in great demand as a shielding gas in the welding industry. However, at the temperature of 4500 degrees, we know from tests which I have observed myself that the carbon dioxide may often break down to some extent and give off some carbon monoxide at the exact point of welding. Though this will probably be rapidly dissipated in the average large shop with ordinary moving air currents, if the work is done in an enclosed space such as a tank or down in a pit, there may be appreciable exposure to carbon monoxide. As far as my studies of this particular young man's

headache have gone, I would say he is probably not malingering but has been made uncomfortable due to a small amount of carbon monoxide or an oxygen lack with excess carbon dioxide down in the pit where he worked. In the few days he had worked he had not been seriously poisoned and there has been no residual.

Another man working in the same pit for five months but making no complaint has admitted now to having so much nausea that he had no appetite and has lost twenty pounds in the last four months. We owe a debt to the complainer who brought the danger to our attention.

When the industrial engineer and I went down into the pit where the second man was at work with the carbon dioxide shielded arc, building up the imperfections in the large steel casting with a two foot rim extending over his head, we found by holding the CO tester at nose level, fourteen inches from the arc, that the CO concentration was 50 to 100 ppm. just below the maximum safe threshold. At seven inches the concentration was 75 to 100 ppm. At five inches the concentration was 600 ppm. and at three inches, 1000 ppm. The readings at seven to fourteen inches showing 50 to 100 ppm. might be safe on a large and open floor because of dilution by air currents, but when down in a pit, in this case eight feet deep and sixteen feet square, with part of the casting making a hood over the patient's head, such diluting air currents would not be present to carry away all the CO.

Furthermore there was a large heating torch on each side of the casting which in itself would consume considerable oxygen and the CO_2 shielding equipment delivered CO_2 at the rate of 30 cu. ft./hour. While there is only a minimal amount of CO, there is additional CO_2 and reduced oxygen. This could account for an honest complaint of nausea, headache, and general "lousy feeling". This must be prevented by forced ventilation.

We do know that in circumstances of danger much more intense than this case that when an individual is exposed to the inhalation of CO_2, such as in "black damp" of an abandoned mine shaft or in the pit of a nearly empty silo he may be rapidly suffocated.

In another instance of unrecognized carbon monoxide exposure, a small shaft was being drilled through a hard-rock hill in Northern Wisconsin. It is known that after blasting, carbon monoxide is formed. In this case a young and inexperienced worker was sent in to set up drilling machinery each time that a blast had been set off. Towards the end of the first week he became confused and dizzy and developed a terrific headache. His fellow workers, three or four of them, loaded him into a car and took him home to his rooming house. They then drove away. The landlady thought that perhaps he had been brought home drunk and was not perturbed by the fact that he did not come out of his room for over 48 hours. At the end of this time she called the fire department who found that the boy was unconscious. Though they revived him quite rapidly with oxygen, he had lain unconscious so long that the carbon monoxide had interfered with oxygen, to the basal areas in the brain, resulting in what is called "central pain". This cerebral area already has a low blood supply and is very sensitive to oxygen lack of carbon monoxide poisoning. It was many months before this man was able to be relieved of his terrible headache that often required an intravenous anesthesia.

Marked weakness and collapse may confuse a physician who feels that such a case may either be a severe anemia due to an internal hemorrhage or perhaps a case of heart failure on a coronary artery basis. A few years ago I was called to see a patient who had suddenly developed a bloody urine associated with marked weakness and anemia. On the invitation of the employer I inspected a small plant employing only 4 or 5 people in a room in a second floor building in a very small country town. They did metal casting and darkening of the casting using aluminum. They placed these aluminum castings in a solution of equal parts of hydrochloric acid and water into which several handfuls of white arsenic were dumped. To indicate how disgraceful the conditions were, which would never be tolerated in a large industry, the white arsenic was kept in open paper sacks on the shelf, like flour in a bakery.

On one Saturday the castings were changed without warning to 100% zinc. The full operation took only a minute, but this was done seven or eight times over a period of two hours with no immediate symptoms. About six hours after this procedure the patient, a high school boy, began to feel nausea, weakness, and noted bloody urine. The next day I was called to investigate the case and had the operation demonstrated to me two or three times over a period of half a minute each time. I sniffed the gas which was evolved and noted the garlic-like odor. Three or four hours later I became very weak and tired out but did not pay any attention to it until twelve hours later when I noted that my own urine was also burgundy red in color. At this time I was informed that the foreman who had shown me the operation had also the same group of symptoms with the same burgundy red urine.

Those of you who recall your high school chemistry remember when zinc is dropped into hydrochloric acid containing arsenic, that free arsenious hydride, or arsine, is developed. This is twenty times as toxic as cyanide. The action of the arsine consists in laking the red cells so that there is a rapid anemia and an associated jaundice as the liver works overtime in attempting to dispose of the broken down hemoglobin.

All three patients are now alive because of the prompt use of the Bristish Anti-Lewisite, or BAL, which was developed to counteract the deadly effects of Lewisite or arsine war gas.

So much for a poison to which three patients were suddenly exposed without warning in a very small country town where there was not supposed to be any industry present, certainly no more than that of cheese making.

Now imagine another dramatic picture of a young man coughing up frothy sputum and barely able to gasp out the cause of his industrial poisoning. About an hour or two before his death, one resident was alert enough to ask him the question, what is your occupation? Five days before this, he stated, he had been asked by his foreman to use an oxyacetylene torch to clean out a cadmium tank in a small plating company. Cadmium had been used in this tank and they wished to transfer back to zinc plating. The cadmium, however, had collected in a rather large lump at one of the electrical poles. After working an hour at this with an ordinary torch, the patient complained of a slight cough and stopped the burning of cadmium. He went home never to return.

Two other maintenance men laughed at the first worker and completed the operation in another hour and a quarter. That evening they both had rather severe dyspnea but recovered after a few days.

Three days later the patient's wife called the plant and reported that he had "pneumonia" and had been taken first to one hospital and then to another because of his critical state. Five days after the original exposure the patient died.

The use of cadmium in the ordinary plating operation at ordinary temperatures is harmless, but when it is fumed by burning, the very small fume particles are inhaled deep into the lung where they have the same effect on the pulmonary alveolar membrane as inhaled phosgene. The result is a diffuse burn of the entire lining of the lung with an outpouring of fluids which cannot be told from the acute heart failure syndrome with pulmonary edema. Positive pressure applied early might have helped, but no intelligent treatment was given because no one knew the sequence of events and the occupational exposure. I myself was first informed of this case long after he had expired, and I was asked to review the whole matter and to recommend proper precautions in the plant in regard to all their industrial operations.

Now let's take another symptom complex which may confront you in the middle of the night as it did me one sultry midnight last summer. The wife of a young and vigorous man called his physician saying that he was suddenly very weak, that he had twitching of the fingers, was nauseated, was dizzy, had a headache with convulsions and had fainted. The doctor ordered him taken to the County Hospital. The resident then called me for suggestions. Inquiry as to the occupation showed that four hours previous to his collapse he had sprayed "parathion" in an enclosed greenhouse in order to kill spiders infesting roses. The patient worked one hour wearing a mask and rubber gloves, but no cap and no rubber coat as it was extremely hot. That was 5:30 to 6:30 p.m. At 9:00 p.m. he came back to open the greenhouse windows. This took him only fifteen minutes, but for so short a time he put on no mask, no gloves, and wore a tee shirt. It should be remembered that parathion, which is the civilian equivalent for the so-called war "nerve-gas", is absorbed not only by inhalation but through the skin, especially a moist hot skin. Parathion has the faculty of very efficiently inhibiting cholesterinase enzyme which normally inactivates the acetyl choline which forms at the end of nerve fibers. With the accumulation of the acetyl choline, the individual has a muscarine-like poisoning. If untreated he often will go on to collapse, unconsciousness, convulsions, and death. The only treatment is atropine given intravenously in heavy doses. Upon my advice the resident gave him a thirtieth of a grain of atropine intravenously every hour from 12:30 until 5:30 a.m. Then he was on the verge of mild atropine poisoning with dilated pupils and excitation so that the atropine was stopped. The patient then became conscious and gradually got over the parathion poisoning. Blood studied for cholesterinase showed a marked drop characteristic of parathion poisoning.

Incidentally, it took two to three more months for the cholesterinase level to approach normal. This point has to be borne in mind in chronic exposure such as occurs in spraying farms with this substance from an airplane. In the Mid-west and West there are many small companies now employing three or four pilots to spray

this type of material over fields as an insecticide. Furthermore, this material can now be bought over the counter by the small do-it-yourself gardener who I am sure has no comprehension of the danger involved.

Another interesting case is that of a young man also working on a very hot night stripped to the waist as a janitor in a small chemical plant. His job was to collect waste papers and smash them down into barrels so that they could be disposed of. On this particular night he had run out of barrels on his own floor so he went upstairs and got three or four barrels there. To pack them tight, he climbed into the barrel and jumped up and down. He noticed that there was some dust in the barrel but he paid no attention to it. He worked with these extra barrels for about an hour before he stopped work near midnight. He went across the street to a tavern and there his friends noticed that his nails and lips were blue, and he himself felt very weak and nauseated. He remembered collapsing but nothing else until he found himself in the hospital. When I saw him there at 3:00 a.m., his mucous membranes were still very blue and cyanotic and he was in a state of collapse. His meta-hemoglobin anemia responded well to treatment with oxygen inhalation. Investigation of the dirty barrels which the man had packed for the last hour of his work indicated that they had contained para nitra aniline. This substance is absorbed through the skin and produces marked metahemoglobin anemia with weakness and cyanosis.

A tentative diagnosis of leukemia had brought another patient to the hospital because of jaundice and marked hemorrhagic diathesis. Finally, a few hours before the patient died of purpura and bleeding from all body orifices, I was asked to see him. When I took his history, really a death-bed statement, I found that some six or eight weeks before he had bought a second-hand cabin cruiser which badly needed repainting. He built a small shelter about it and proceeded to remove the paint using gallons of the paint remover. We know that many paint removers contain at least 50% benzol. Two or three weeks after he began this part-time work he developed marked weakness and jaundice. Examination showed a definite anemia with a depression of white cells as well as the red cells. Though there are now many relatively safe substitutes for benzol in paint removers, benzol is still so much more effective and cheap, it is to be suspected until proved otherwise that benzol is the culprit when we see such a case history.

Now let us imagine that we had been called to see a young man ill with abdominal distress and difficult vision associated with headache. This is the history that he gave me when I was called to see him five days after he went to the hospital. Four days previously his boss, a small linoleum floor laying contractor, employing three or four men, had sent this man out to pull up, patch and relay linoleum in a small basement apartment. While the man had always used gasoline previously to take off the cement underneath the linoleum which he would then relay, this particular morning of October 21, the boss insisted that the patient use a new, much more effective solvent. The patient worked eight hours on his hands and knees in the basement using ¾ of a gallon of this material to take the cement from the linoleum. The next day he got up with a headache and was dizzy and nauseated. After two more days, he called his doctor who put him into the hospital on October 25 because he could not see while trying to read a newspaper, and he was also nearly anuric. When

I first saw him he had already received ample fluids, much too ample, because these patients usually die of fluid retention and pulmonary edema. I advised concentrated glucose with a reduction of fluids, but by November 1, the patient began to develop pulmonary edema and three days later, on November 4, he was dead. Post-mortem showed that the cause of death was:

1. Acute toxic nephrosis
2. Acute myocardosis
3. Acute hepatitis.

The ¾ of a gallon of the clear fluid and excellent solvent which the patient had used as a linoleum cement remover, the nature of which neither he nor his boss knew, turned out to be carbon tetrachloride.

In my city we have many grain elevators for developing those famous refreshing drinks. In the grain there are many weevils. One of the most effective medications used to deweevilize the grain is a fluid called Weevilcide, a gallon of which is put into the elevators with each five feet of grain. The worker involved in this history did not like the odor of the Weevilcide and was given a respirator. Unfortunately, this was a dust respirator which did not keep out any of the vapor. He was a maintenance man in a crew of three. At times he had to clean out grain elevators that became nearly empty and the solvent settled to the lower part where it was very strong. Once after working two or three consecutive days he became nauseated and was sent to a doctor who discovered albumin in his urine for which the physician prescribed two weeks rest. However, when the patient noticed that urination was becoming scanty and nausea was increasing, he was sent to me for the first time for study. Liver tests showed no abnormalities and with no excess resort to intravenous fluids, the urine gradually became normal in amount and clear of albumin. Investigation finally revealed that the Weevilcide contained a large percentage of carbon tetrachloride.

A third experience with carbon tetrachloride shows the careless use of this material by a cleaner of machinery and motors. The patient in question had worked three or four days, along with three or four men, cleaning the grease off some second-hand machinery in a small boiler repair shop. The patient used most of the material himself including four or five gallons of carbon tetrachloride on each of the four days, throwing it on with brushes and rags. The fourth day he was so weak that he had to be sent home and two days later he was hospitalized in a private hospital. As anuria tendency developed, he was then admitted to the County Hospital where he was dialyzed on the artifical kidney because the urine output had dropped to 125 cc. for each of two days. The NPN had risen to 380. Ten days later the patient began to receive oral fluids and responded well, though he then developed a temporary hemorrhagic diathesis. The patient also had every evidence of involvement of the renal tubules with a nephrosis. This lasted for nearly a year before he was able to return to work.

All of these three cases, then, developed lower nephron nephrosis and in all instances the material was being used with no idea that it was toxic. In reality carbon tetrachloride is one of the most dangerous poisons known to both modern industry and the home. However, any child can buy a bottle over the counter at a drug store.

Turning to other apparently milder symptoms when patients have a simple complaint of diarrhea, we usually think of so-called intestinal influenza. During the last war I was asked to study a group of five or six men in a small operation where bichloride of mercury was developed in a war product. These men had so-called intestinal influenza according to their foreman, but also they had a very foul breath due to a severe gingivitis. Investigation showed that mercury was being heated in a silica retort with free chlorine to form bichloride of mercury in the manufacture of mercury dry batteries. All went well until the demands of the Armed Forces required increased production. This meant increased heat and turning up of the Bunsen Burners under the silica retorts. As a result there was frequent cracking of the retorts and spread of the mercury vapor and chlorine into the small room. Respirators were furnished but the men rarely took time to use them as they replaced the retorts. The diagnosis probably would have remained intestinal influenza had not one of the members been a temporary worker whose wife demanded vigorously that he be investigated for his very foul breath. After a month's work at the above operation he finally quit work because of marked soreness of the gums and swollen neck glands. One of his fellow workers had severe diarrhea so that he passed clear blood in the stool.

Physical examination of four of these men showed a very fetid breath with swollen inflammed gums. Though none of the four cases showed any evidence of renal involvement, one showed rather typical "erethism" or nervous involvement such as was described in *Alice in Wonderland* in the person of the Mad Hatter. All had increased mercury in the urine. Unfortunately these cases were studied before BAL was available for treatment except for the Armed Forces. Removal from exposure and treatment of the gingivitis with penicillin removed the wife's presenting complaint of bad breath. Time had to cure the mercury poisoning, though we called it expectant treatment.

Sometimes it has been my experience to know nothing of these cases until I have been asked to review the post-mortem findings. The following incident is such an example. The manufacture of an "oil-free" or self-lubricating bearing seemed to be the answer to prayer for a certain small machine shop in Milwaukee which needed a new operation to expand its activities in order to keep the men busy. Four or five men were detailed to the new operation. This involved boring holes in bronze bearings, then closing up the holes with a waxy filling containing a secret formula. This acted very efficiently as a permanent self-lubricating agent for the bearing. After the material had been placed in a number of holes in the side of the bearing, the bearing was then placed on a lathe and the surface ground down with a file. The black dust evolved was so concentrated that within a minute or two after the man started the grinding operation his face became completely black. Now a dirty face is not necessarily an indication of danger, but it does indicate a concentrated exposure to dust. It has to be proved in each case whether the dust is poisonous.

Neither the owner of the small shop nor the operator knew the true contents of the secret formula so no effort was made to prevent the inhalation of this dust. For several weeks prior to stopping work one of the employees had a recurrence of an old ulcer complaint. He was admitted to a hospital for treatment about six months after he had started grinding the oil-free bearing. Upon admission he developed a

constant pain in the back of the head and neck with marked restlessness so that it was felt that he probably had a brain tumor. However, just before the operation, laboratory studies showed that he had marked basophilic stippling and secondary anemia. Re-examination of the gums then showed that he had a marked lead line. The urine showed lead also. These new developments suggested that the man might have lead encephalopathy for which he was given calcium gluconate intravenously. However, the decompression was done to relieve pressure within the skull, four days after the patient came into the hospital. He died within a few hours.

After the post-mortem was done I was called in for the first time, to investigate the case. I then found that the secret material combined in the wax and carbon mixture which produced the self-lubricating effect on the bearings was 90% lead oxide. This is simply another example of this commonest and most insidious poison in industry. As some of you may know, I have been working with lead since I first had the chance to study six cases here at the Ford Hospital over thirty years ago.

Following this disastrous episode, the employer and his insurance company took vigorous steps to reduce the possibility of inhaling any of the lead dust at the grinding or buffing operation. Air analysis subsequently showed an entirely safe level of lead in the air at this operation so that when I re-examined the three or four other patients involved, I found no evidence of lead in blood, urine, and of course no lead line of the gums. However, not long afterwards a poorly educated man was put on the operation at night. The importance of using all precautions to reduce dust at this operation was not taken seriously by him. After two months of working nights with no supervision, he began to be absent from work because of indigestion. The employer who by this time was rather sensitive to gastrointestinal complaints at this particular operation sent him down to me for study. I found that he had a 12 plus lead line and many stippled cells as well as a 4 plus porphyrin in the urine. Fortunately by this time Calcium EDTA was available and we deleaded him thoroughly with the usual marked increase of lead in the urine, in his case rising from .2 to 13.3 mgs. of lead in 24 hours immediately after he started the first course of Calcium EDTA given intravenously. Oral medication with Calcium EDTA is practically useless, in my opinion.

Two or three years ago in the midst of a lecture at the Medical School I was called out to take an emergency telephone message. An excited voice stated that I must see him at once because his physician had told him that he had lead poisoning. When I saw him that afternoon at the hospital, I found that the diagnosis was correct. The patient had a marked lead line, many stippled cells, 86 per 50 fields, and lead in the urine. An interesting fact was that this man was the superintendent and part-owner of a small brass foundry employing seven other men. Besides the superintendent, five others of these men had marked lead absorption. The brass foundry had been in operation only six weeks, pouring brass without any respirators or any ventilation. The brass contained 10 to 12% lead. Of eight employees working, six had heavy lead absorption and three of these required hospitalization including the superintendent I have just described. At my request the plant was closed until proper engineering study could be done and ventilation control had been checked by the Industrial Hygiene Unit of the State Health Department of Wisconsin. After two or three

weeks, the plant resumed work with proper ventilation and respirator control. Then all men were able to return to work pouring brass.

One summer night a confused colored man wandered into our County Hospital complaining bitterly of headache. He was so confused that no history could be obtained. Spinal fluid was negative and the patient was treated expectantly. After about a week, laboratory tests showed a secondary anemia with 200 stippled cells per 50 fields and the laboratory technician suggested that the physicians study the gums for a lead line, and that perhaps they had better call me. We found that he had a marked 12 plus lead line. After much careful questioning and investigation an astute resident found that the patient's occupation was that of an operator of a waste paper press in a small junk shop employing only three men. This shop received, however, the trash paper from several large neighboring companies. The paper was heavily contaminated with lead arsenate and other lead compounds. No respirator or suction had been provided for the individual as he and his employer had never thought of the possibility of lead exposure. As he put the lead contaminated trash paper into the press, he would get in to jump up and down to pack the paper in. Of course, this caused evolution of much lead dust. At the first admission the patient was given only expectant treatment and up-building therapy with iron. He was also advised to stay away from this type of lead exposure.

However, a few months later it was found that he had returned to the same work. All his symptoms recurred so that he was then started on the new treatment with Calcium EDTA. This caused a rise of lead in the urinary excretion per liter from .6 to 6.0 mgs. per 24 hours. Since apparently it was hopeless to control the working conditions in this small plant, the patient was advised to find work elsewhere.

Not long afterwards at the same County Hospital, a Puerto Rican who could talk very little English, appeared complaining of headache and inability to feed himself because of marked weakness of both wrists. Our investigation showed that he had been employed for five years as a grinder on brass castings with only 2 or 3 other workers in a very small brass foundry. Brass contains 5 to 30% lead.

This patient had been operated on previously, not only for appendicitis but also twice for alleged recurrent intestinal obstructioin which was quite possibly recurrent lead colic.

On physical examination it was found that he had a lead line and that there were many stippled cells, increased lead in the urine together with bilateral wrist drop. Following several courses of Calcium EDTA, the abdominal symptoms have disappeared, anemia has cleared and the bilateral wrist drop has been practically cured so that he is now able to return to his original work, though he will now wear an approved lead respirator.

From these three cases alone it is apparent that contrary to the general impression, lead poisoning is still frequent. Lead rarely kills and even the small industry can use it safely. Carbon tetrachloride, on the other hand, should not be permitted in large or small industries.

These two hazards have been recognized for many years but new processes and new chemical compounds daily challenge the engineer and physician team.

In summary, it should be obvious that every physician should still ask the question of his patient originally propounded by Hippocrates, "How are your bowels?" In our more modern industrial age, he must also ask one more question, "What is your trade?" just as Ramazzini, the Father of Occupational Medicine did 250 years ago when he used to descend into the pits to study first-hand the operations of seventeeth century industry.

Surely when we are called out to see a new medical emergency in the middle of the night, we should always make sure of the occupation. The acute pulmonary edema may not be a simple heart failure as it seems to be on first glance, but really may be due to the inhalation of ozone or cadmium fume. Headache may be due to carbon monoxide or lead. Convulsions or collapse may not be epilepsy but may be parathion or para nitra aniline poisoning. Marked weakness and anemia may be due to benzol or lead and not pernicious anemia or leukemia. The bloody urine may not be due to a renal stone but may be from benzol or arsine poisoning. An anuria tendency with high blood pressure, nausea, jaundice, loss of vision and headache may not be a simple chronic nephritis on a post-infectious basis but may really be a carbon tetrachloride intoxication.

Bloody stools, too, may not be intestinal influenza or even ulcerative colitis but may be due to an acute mercury intoxication. Finally, the chronic abdominal distress accentuated by occasional violent abdominal colic and rarely complicated by wrist or foot drop may not be merely an acute appendicitis or intestinal obstruction, but really heavy lead absorption and lead intoxication.

In the face of this expereience of mine and that of many others in occupational medicine, the following conclusions seem inescapable:

1. It is imperative to insist on a good occupational history as a part of every differential diagnosis. We should be particularly careful not to make a careless diagnosis of malingering.
2. This occupational history should be confirmed by first-hand observation of the patient's work station right out in the plant by the physician-consultant working hand in hand with the engineer. Thus if we know with what we are working, they can handle any poison safely.
3. We should know the basic mechanism of the action of a poison, both as to its portal of entry and to its point of attack on a particular organ, whether it be on the central or peripheral nervous system, liver, kidney, bone marrow, or heart.
4. Prevention is the best treatment because specific therapies are few, though in appropriate instances described above, these may be oxygen, atropine, BAL, and most recently Calcium EDTA, or calcium ethylene disodium tetra-acetate.

5. The physician can easily become familiar with common sense good plant-housekeeping as well as the general principles of proper ventilation together with protective equipment such as adequate respirators.
6. If placement and periodic re-examination studies are planned and carried through by the physician, they will make him an irreplaceable adjunct to small industry.
7. Finally, all physicians should realize that occupational medicine is preventive, internal medicine applied to industry.

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THE VALUE OF THE PAPANICOLAOU SMEAR TEST*

ZEPH J. R. HOLLENBECK, M.D.**

Clinical experience and research in therapy of cancer of the female genitalia and especially of the cervix have given us much with which to work. We have radio-isotopes: super-voltage x-ray: teletherapy; radical surgery, and above all, we have a tremendous store of knowledge in methods of application of all of these. And yet, when we consider all cases of the most common cancer of the female genitalia — cancer of the cervix — more than 60% of them do not live 5 years (after the diagnosis is made.)

When we look at the results of treatment year after year and decade after decade, we are not startled by the improvement in these results because they have been slow to make their appearances: but one thing is very much in evidence. It is the fact that as in all types of cancer, the earlier in the disease that therapy is begun, the better are the results.

In addition to public education, which has improved this feature of the whole picture, we need a method to detect cancer early. In other words, we need a "case finder". We have it! We have it! At least, we have one method — the Papanicolaou smear test. We have it, and we have had this tool for some time — but it has *not* been widely used. It will do little good to print it here unless those who read this put it into practice. William Stewart Halstead once said, "conceptions from the past blind us to facts which almost slap us in the face."

It is our belief that every woman should have a pelvic examination and a vaginal cytology study at least once every year. I will outline briefly the results of a survey which has led us to an even stronger conviction in this belief.

A country-wide cancer survey project using the Papanicolaou smear as a screen test has been in operation in Columbus, Ohio for the past year. This has been done under the co-directorship of Dr. John C. Ullery, Chairman of the Department of Obstetrics and Gynecology and Dr. Emmerich Von Haan, Chairman of the Department of Pathology of the Ohio State University, and with the aid of a grant from the United States Public Health Service.

A similiar survey has been in progress in Memphis, Tennessee for the past three years. The Memphis survey study has found 527 carcinomas in 70,000 examinations or an incidence of 0.75% (1 in 143). In the Columbus survey, we have found 99 carcinomas in 35,394 examinations or an incidence of 0.279% (1 in 357.)

The source of the material for examinations has come from private physicians (27,669), The Cancer Survey Clinic (3,169) and from other clinics (6,675).

The method of making the test is simple and painless. The material from the posterior vaginal fornix is removed with an aspirator and placed on a glass slide.

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**From the Department of Obstetrics and Gynecology and the Department of Pathology, The Ohio State University, Columbus, Ohio

This is covered with another slide, and the two are slid apart. The second specimen is prepared after the vaginal speculum is in place by scraping the area around and in the external OS of the cervix with a tongue depressor or a wooden scraper designed for this purpose. The material obtained is placed on the slide, and the slides are fixed and transported to the laboratory in a mixture of equal parts 95% alcohol and ether.

In the Columbus study the "aspiration only" method is being used with a control run by a designated few physicians who are using both the aspiration and scrape. 37,540 aspirations and approximately 5,260 aspirations and scrapes have been surveyed. Eleven (11) patients with cancer were found on positive scrape smears that were negative on aspiration.

In applying this test in your own practice, your cytologist may report his findings in one of three ways: by class, by cytology or by interpretation.

CLASSIFICATION OF PAPANICOLAOU SMEARS

CLASS	CYTOLOGY	INTERPRETATION
I	Normal	Negative
II	Atypical, No Evidence Malignancy	Negative
III	Suspicious, Suggestive — Not Conclusive	Suspicious (Positive)
IV	Strongly Suggestive	Positive
V	Conclusive of Malignancy	Positive

The suspicious or positive smear demands an adequate biopsy of the cervix, preferably by cold knife conization, a D&C and an adequate pelvic examination under anaesthesia. It must be emphasized here that this test is not infallible, and a negative report in the face of symptoms or positive, clinical findings means absolutely nothing. A patient presenting a suggestive history or suspicious or presumptive findings must have adequate biopsy and examination. This sequence of events, symptoms with negative smear, usually occurs in endometrial cancer.

We must also remember that a positive smear is by no means an indication for therapy. Definitive cancer treatment must be initiated only as a result of a positive biopsy.

In one year, from May 1, 1956 to May 1, 1957, there were 99 cancers of the female genital tract found in our survey of 35,394 women; the various types of carcinomas are as follows:

MAY 1, 1956 — MAY 1, 1957

Carcinoma of the Cervix (Three — Cervical Stump)	52
Carcinoma of the Corpus	12
Carcinoma in Situ — Cervix (One during Pregnancy)	31
Carcinoma of the Vagina	3
Carcinoma of the Ovary	1
TOTAL	99

Most of these tumors were unsuspected, but to appreciate the full and tremendous value of the routine Papanicolaou test in detecting 83 cancers of the cervix (of a total of 99 carcinomas), it is well to remember again the International Clinical Classification of Cancer of the Cervix. Stage 0, Microscopically No Invasion (intra-epithelial); Stage I, Limited Clinically to the Cervix: Stage II, Extending Beyond the Cervix but not to the Lateral Pelvic Wall (may also involve the upper 1/3 of the vagina): Stage III, Extending Laterally to the Pelvic Wall (or extending below the upper 1/3 of the vagina); Stage IV, With Distant Metastasis (or a frozen pelvis or bowel or bladder fistulization due to tumor).

The 83 cervical cancers were classified clinically as follows:

Stage 0	31
Stage I	40
Stage II	4
Stage III	6
Stage IV	2
TOTAL	83

To further appreciate the value of the Papanicolaou smear we must look at our present results of therapy. These statistics from the Department of Obstetrics and Gynecology of the Ohio State University compare favorably with nationwide and world wide publications of survival rates.

FIVE YEAR SURVIVAL	
Stage 0	96.2%
Stage I	81.4%
Stage II	48.5%
Stage III	21.4%
Stage IV	2.5%

With these survivals of the various clinical stages of cervical cancer in mind, let us now compare the difference between the registrations in the tumor clinic at the Ohio State University Hospital ten years ago with the cases found by means of a mass survey during the year just past.

1947	Stage	1957
0%	0	38%
14%	I	48%
41%	II	5%
41%	III	7%
4%	IV	2%

This is truly progress.

Cancer of the cervix has three clinical characteristics that are extremely important in appreciating the value of the Papanicolaou smear test. First, it is, by far, the most common cancer of the female genital tract. Second, relatively good results are obtained if adequate treatment is instituted early. Third, it is the easiest to detect early of all the cancers of the female genitalia.

This test can be applied to anyone's practice who treats women. One way to reduce the 60% mortality rate from cancer of the cervix is to use this simple test routinely.

It seems then that your mother, your wife, your daughter, your sister, yes — every woman deserves and should have a pelvic examination and a "Cancer Smear Test" at least once a year.

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THE HOME MANAGEMENT OF THE POLIOMYELITIS RESPIRATOR PATIENT*

THAD H. JOOS, M.D.

While the number of new cases of severe bulbo-spinal poliomyelitis have decreased since the Salk vaccine, there still will occur a number of cases in the non-immunized group and in addition there are many affected persons remaining from the pre-vaccination period. This report deals with the management of this latter group by myself, as a private physician, during the one year period between July 1956 and June 1957.

There are six patients in the group, five of whom are post poliomyelitis patients and one with progressive dermatomyositis. All but one use some form of respirator aid and this one is a potential user. Their ages range from one year to 36 years. The relatively advanced age points out once again the severity of poliomyelitis in the young adult. Four of the five patients with poliomyelitis residuals are married and they have a total of eight children among them. The average time since the onset of poliomyelitis has been 2.9 years.

Equipment used varies from patient to patient but only one, the dermatomyositis patient, uses a tank respirator. The remaining are sufficiently well ventilated with a Chestpirator or Rocking Bed. In addition, there are slings for feeding where indicated and other such useful adaptive apparatus. In general, the patient and equipment take the better part of a 10 by 15 foot room.

The vital capacities of these people ranged from 8% to 30% of their expected normals. This great decrease in respiratory function makes lung infections their major medical problem. A total of 13 such infections occurred, 10 of which were treated at home while three were severe enough to warrant hospitalization. Home therapy consisted of antibiotics, usually intramuscular penicillin, given by a member of the family, or oral chloromycetin for from 5 to 7 days. Steam, nose drops, and an increased use of the Chestpirator, were also employed. Those using glossopharyngeal breathing[1] as an aid in coughing experienced in general less difficulty in recovering from the infection.[2]

Next in illness importance were those related to the genito-urinary system where calculi made pain and infection commonplace. Three episodes of colicky pyuria of a serious nature were encountered and all needed hospital therapy. One patient with several large calculi subseqently underwent a uretero-lithotomy[3] and is now symptom-free six months later.

When considering the totalness of the patients' disability, the small number of hospital admissions seems to me quite remarkable. Home visits and office consultations were equally low totaling only 20 for the entire six patients.

The purely medical problems are by and large easily handled, but the impact of such an illness on the family as a unit is one which tests the resourcefulness of all

*Given before the Henry Ford Hospital Medical Association, May 31, 1957.

concerned. Life in the immediate post-acute disease phase has often been relatively easy, being spent in a Respirator Center, where many similar patients are undergoing a program of extensive rehabilitation. Home life following this period can, on the other hand, be extremely trying where the roles of provider and mother are being played alone by the well mate in the married patients. Full-time attendants or housekeepers are used in most of these situations but "outsiders" can never perform and guide the home functions as would the disabled parent.

Activities outside of the home are few because of the immobility of the patient. Two of the six are ambulatory to a degree but truly public appearances are unusual because of self-consciousness. Only one patient, the most severely paralyzed of the group, uses a wheel chair and eats regularly at the table with his family. The effort needed to make this possible is considerable.

Diversion inside the home usually is simple, with reading and television being the principal ones. Gainful employment of some sort is being accomplished by all three adult males. One is working up a sizeable magazine subscription and Christmas card enterprise. Another does part-time accounting at home, while the third composes copy for classical music programs on a local radio station. The teen-aged girl with dermatomyositis is a talented artist, painting with a mouth stick. She graduated from high school in June 1957.

PROGNOSIS

There have been selected patients who have survived up to 20 years with such low vital capacities as the present group, so that the short term outlook for life is good. Death, when it comes, most frequently is a result of respiratory system complications such as bronchopneumonia, lung abscess, and atelectasis. Gastro-intestinal bleeding and acute gastric dilatation are also prominent causes of death. The sequellae of chronic kidney infection rank third as reasons for the patient's demise.[4]

SUMMARY

The medical management in these patients does not differ from that of any chronic disease in that meticulous attention to their many needs and an understanding of their peculiar problems will lead to a definite, comfortable prolongation of life.

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THE IMPORTANCE OF EARLY DIAGNOSIS IN NARROW ANGLE GLAUCOMA*

MALACHI W. SLOAN II, M.D.

Glaucoma is a disease or a number of diseases in which the intraocular pressure is elevated above normal. Today we shall confine our discussion to primary glaucoma which eliminates all those secondary to trauma, neoplasma, primary infections, etc. To give a definition of primary glaucoma that illustrates this phase of the subject, the following simplification is made.

An eye which is healthy and has a normal intraocular pressure is one in which the amount of aqueous flowing in equals the amount of aqueous flowing out. If the outflow becomes obstructed and the inflow remains the same, the intraocular pressure rises; or if the resistance to outflow remains the same and the inflow increases, the intraocular pressure will rise.

We have two primary means of medically controlling this pressure. One is by the use of Pilocarpine or other miotics in which the outflow is increased. The second is the use of Acetazoleamide (Diamox) orally which suppresses formation of aqueous and thereby reduces the intraocular pressure. If the combination of these two methods fails to control the tension of the eye, then we resort to surgery to (1) form another outlet, (2) create freer access to the normal outlet, (3) reduce inflow or (4) some combination of these.

As in all diseases, the earlier the diagnosis is made the better the outlook for the patient. I believe the evidence I am about to submit shows the importance of the role played by the ophthalmologist in detecting early glaucoma. It is an insidious disease which at first is practically symptomless. This may remain true almost up to the time when vision fails completely.

In 1,184 routine refractions done on patients 40 years of age and over in the past 14 months, there were 46 with an elevated tension, an incidence of 3.8%. Elevated tension was disclosed by taking routine measurements with a Schiotz Tonometer. This instrument has a foot plate which rests upon the cornea and a plunger which sinks into the cornea a varying distance, according to the resistance afforded by the intraocular pressure. The amount it displaces the cornea inward registers on a scale. This reading is translated into millimeters of mercury of intraocular pressure.

At the conclusion of each of these 1,184 routine refractions, with eyes still under the influence of full mydriasis or dilatation, tensions were taken. Forty-six patients showed elevations of 26 or over. Of this group, a diagnosis of glaucoma subsequently was established in 31 patients; 12 are currently glaucoma suspects and in 3 the possibility of glaucoma has been ruled out. Thus one sees that 43 unsuspected cases

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of elevated tension would have been missed had they not been screened by routine tonometry.

Before we pass onto the classification of glaucoma, let us consider momentarily some of the theories on the causes of glaucoma. Up until the past few years all we knew was that aqueous entered the eye largely via the ciliary body, flowed into the anterior chamber through the pupillary area, then out of the anterior chamber into the Canal of Schlemm and from there passed into the general circulation. Many theories have been postulated in the past hundred years dealing with the electrolyte balance, the molecular pressure, hydrostatic pressure and osmotic pressure as they are related to the blood aqueous barrier, etc., as well as the mechanical situation. All of these theories can be classified under two main headings, the mechanistic theory and the neurovascular theory. There is no doubt that each theory has an element of truth but since the latter does not lead us toward a different or better treatment in our present scientific status, I have become an advocate of the mechanistic theory.

This theory does force us to analyze the cause of each case of glaucoma. This in turn guides us to a more logical management of glaucoma. This group temporarily discounts the neurovascular theories and explains glaucoma on the basis that the fluid cannot get out either because of obstruction to the outflow at the root of the iris or by changes in the wall of the eye which prevent the aqueous from passing through it. It is my wish to keep the classification simple and at the same time make it practical so that a better pattern of treatment can be developed. I have adopted for my use Kronfeld's classification. He divides all eyes:

Situation A — a deep anterior chamber and wide roomy angle

Situation B — a fairly deep anterior chamber but the angle is narrow and the iris has an appearance of an iris plateau.

Situation C — a shallow chamber and the angle is narrow throughout.

My first step after detecting an elevated tension is to attempt to classify the eyes into Situation A, B, and C. Situation A and C can be readily determined by inspection alone. First with the slit lamp which shows the depth of the anterior chamber and then with the gonioprism (which brings the angle of the eye into view), either the angle is very wide and roomy or it is narrow and pinched. This then classifies two groups characteristically — a Situation A and a Situation C. Situation C is typically a small, hypermetropic eye, and it is so characteristic that even the unscientific casual observer notices it.

Situation B remains. These cases must be sifted out and it must be decided which one belongs in A or C as far as their glaucoma mechanism is concerned. For this purpose I use two provocative tests. First, a mydriatic, which in the case of Situation C closes the angle and precipitates a rise in pressure thus confirming it as a narrow angle glaucoma. If a mydriasis has no effect, but upon drinking one quart of water on a fasting stomach and then taking the tension half an hour later,

the tension rises 8 m.m. of mercury or more, the test is indicative of potential wide angle glaucoma. Obviously, the obstruction is then located in the wall of the eye in the filtering system located in the angle.

In the past five years there has been the development of another method of studying the intraocular pressure known as tonography. This is where an electric tonometer, basically more precise than the usual mechanical Schiotz Tonometer, is hooked up with a recording device. When the foot of the tonometer is placed upon the eye and held there for a period of four minutes, a tracing is made. This tracing gives us a measure of the facility of outflow of the eye. That is, we can calculate from it the approximate volume of aqueous which flows out of the eye per minute per millimeter of mercury pressure. Tonography has a fairly large percentage of error, so one tracing often does not clinch a diagnosis. By taking tonograms when the patient is under miotics or after ingesting a quart of water, the appearance of the tonogram and the changes of the facility of outflow does materially aid us in telling the type of glaucoma that exists or whether glaucoma is present or absent.

The last and one of the oldest means of evaluating the state of an eye with glaucoma is by visual fields. However, in narrow angle glaucoma, changes may not occur until very long after diagnosis is possible by other means. Fields only show the extent of damage to the eye up to that time.

Narrow angle glaucoma which is not diagnosed means the development of anterior synechia. This means a reduction in the access of the aqueous to the filtering system which is contained in the wall of the eye. When the iris becomes pushed up against the posterior surface of the cornea, the entry way to the filtering system in the wall of the eye located at the limbus is obstructed. Then results rises of intraocular tension ranging from minimal and symtomless to moderate subacute attacks associated with some pain in the eye and blurring of vision. When pressure rises greatly, there developes an edema of the cornea, such as seen in an acute glaucoma attack. The edema is not confined to the cornea but involves the sclera, the entire angle of the eye including the ciliary body, thus the entire filtering system is involved. The filtering system consists of the trabeculae, then the Canal of Schlemm, the anterior collecting chambers, and finally the aqueous veins which dump into the veins themselves.

Having established whether the eye is a narrow angle or a wide angle, we then pass to the treatment. In the event that a wide angle glaucoma is detected, the treatment is not fully satisfactory whether it is medical or surgical. Since surgical treatment is often disappointing, the accepted procedure is to treat the wide angle case medically as long as possible. When evidence of deterioration of the eye appears, that is, visual field changes and uncontrolled tension, surgical intervention is adopted. In general it is accepted that filtering operations are about 66% successful. Thus, one can see that in wide angle glaucoma the treatment leaves much to be desired.

The treatment of very early narrow angle glaucoma is far more satisfactory because in narrow angle glaucoma the chief difficulty is obstruction of the aqueous in

entering the filtering system. In this case a miotic pulls the pupil down to a pinpoint and also pulls the iris root away from the trabeculae, thus opening the angle wider. Everyone agrees that there is such a thing as iris block glaucoma or closed angle. This has been repeatedly demonstrated clinically and in the laboratory. But if the angle is narrow but open, then there is a great difference of opinion as to whether this can be causing the rise of pressure or not. It is my feeling that a narrow angle, though it may not be closed, does produce a relative block or closure angle glaucoma. For example, if people are passing through a doorway which is wide open, the doorway is being used to the maximum benefit; however, if the doorway is fixed to halfway open, everyone knows that only a fraction of the original number of people can pass through that doorway at the same time as they could if the door were wide open. I feel this is similar to a narrow angle eye.

In a typical narrow angle in a hyperopic eye, where intermittant closing of the angle occurs, obstruction to the entrance of the filtering system can be completely relieved by making a small peripheral iridectomy or an opening in the periphery of the iris. If the narrow angle glaucoma is not treated, then the repeated assults of slight edema produce permanent irreversible changes in the angle. Then, when this eye begins to show deterioration, a peripheral iridectomy will no longer be curative, but a filtering operation would be indicated. For this reason I feel that the narrow angle glaucoma should be detected as early as possible and the patient immediately be subjected to prophylaxis in the form of a peripheral iridectomy. If he will not agree to this, he must of course be kept on a prophylactic medical regime of miotics, to prevent an acute attack of glaucoma.

In the past eight years I have operated 38 eyes which I had diagnosed as having narrow angle glaucoma. 33 of these were successful, that is their tension has remained normal since surgery without any medication whatsoever. Four have been improved, that is the pressure remains under control with miotics. One received no benefit at all, but actually has been worse.

In again looking at an angle of an eye which is magnified, it will be noticed that the more narrow-angle the eye is, the more cramped are all of the anatomical parts. The suggested location for a scratch incision in performing a peripheral iridectomy, is 2 m.m. back of the limbus underneath the conjunctival flap. In the extreme narrow angle case this incision may open up just over the ciliary body and one may fail to establish communication with the posterior segment of the eye. Therefore, I suggest that the incision be made at the limbus as far forward as is possible under a conjunctival flap so that the incision opens into the anterior chamber for sure. As the incision penetrates, the iris immediately prolapses into the wound.

A frequent technique is that of sweeping the angle of the eye throughout 180 degrees to break up any anterior synechia which have formed. It is my feeling that such a procedure makes a peripheral iridectomy equivalent to a filtering operation and, therefore lowers the percentage of success. If a simple peripheral iridectomy is performed without any instrumentation into the anterior chamber, then one can figure on 95% success; that is, complete relief from glaucoma.

According to my classification of 31 established cases of glaucoma, there were 4 that were wide angle, 22 that were narrow angle, and 5 unclassified. Thus approximately 70% can be relieved by a peripheral iridectomy. Therefore a small residium of glaucoma will remain to be treated conservatively and in a somewhat unsatisfactory way until our knowledge progresses considerably further than it is at this moment.

In summary an ophthalmologist's examination should include routine tonometry. This examination is essential to a general physical examination performed on people 40 years and over. Secondly all cases of a slightly elevated tension, i.e. 26 or higher, should be investigated further. Upon investigation they should be classified into narrow angle and wide angle, and the patient with a narrow angle glaucoma should be given the choice of an early surgical peripheral iridectomy, which can be curative or the medical regime. And last, treat all wide angle glaucoma conservatively or medically since surgical treatment is unsatisfactory in one third of the cases.

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FATAL SPONTANEOUS HEMATOMA OF THE VULVA IN A PRIMIPARA AT 36 WEEKS GESTATION BEFORE ONSET OF LABOR

PETER H. MULDER, M.D.

The occurrence of this condition which was described by Williams[1] as a "Tumefaction resulting from the escape of blood into the connective tissue beneath the skin covering the external genitalia", is an infrequent complication of pregnancy. This condition was first described by a Frenchman named Deneux[2] in 1830. DeLee[3] describes it as "blood vessels, particularly the veins in the pelvis which may burst during pregnancy, labor or in the post-partum period".

This 23 year old married white primipara was admitted to Wayne Hospital, Greenville, Ohio on February 1, 1953.

The chief complaint was acute hemorrhage into the left vulva. The patient was carried into the hospital by her husband as an emergency, in severe shock. This occurred suddenly at home at noon on a Sunday, February 1st, following what the patient described as "something coming out of her". The husband thereupon looked at the perineum and discovered an acute discoloration, bluish in nature, in the left labia.

The present illness may have begun as early as four days before admission when the patient first noted a slight twinge of pain in her left hip. This subsided spontaneously and was not thought of again. On the day before admission, following an all day journey by automobile over parts of this rural county on the occasion of the death of a grandmother, the patient arrived home late Saturday night and noticed sharp, severe, short, recurrent cramp-like pains in her lower abdomen. This cramping persisted throughout the night, interfering with sleep.

The patient was seen the following morning, the day of admission at approximately 9:00 a.m. The complaint was as described above, that is — sharp, severe recurrent cramp-like pains in her lower abdomen, and the first impression was that of premature labor. However, on further examination, it was found that the uterus was not partaking in any contractions. The lower abdomen showed moderate tenderness on palpation, particularly in the neighborhood of the bladder. It was the impression at the time that the presenting part of the fetus, which was felt to be the head, was somewhat lower than usual for a primipara. The external genitalia showed no evidence of abnormality. The cervix was not dilated, nor effaced.

The patient also complained of a "bearing down" feeling and "feeling of pressure in the neighborhood of the bladder". There was no burning or pain with urination and there was no definite hesitancy or inability to pass urine. There had been the usual bowel movement the day before. There had been one episode of nausea and vomiting, approximately three hours before this examination.

The diagnosis was not established and the patient and her husband were instructed that if any change occurred, they should notify us immediately.

The past history was as follows: She had her last menstrual period May 22, 1952. The expected date of confinement was February 28, 1953. She was a gravida I, married approximately one year. The history of the present gestation was not remarkable. There was a moderate nausea during the first trimester, but further history by systems was not remarkable. Her prenatal physical examination on September 6, 1952 showed her height to be 5 ft. 1 in. and her weight to be 109 lbs. and no physical abnormality. There were no varicosities of the vulva nor of the legs. Serology drawn on the 9th of September, 1952 showed negative Wasserman and positive RH factor. The last pre-natal visit at 32 weeks gestation showed a gain of weight to 127-½ lbs., a blood pressure of 110/70; height of the fundus to be 22 cm., position of the fetus back to the right and occiput presenting; fetal heart tones 132 in RLQ and urinary findings within normal limits.

The patient was admitted to Wayne Hospital, Greenville, Ohio at 11:50 a.m. Sunday, directly to the labor room. Upon first examination, the patient was found to have a large, exquisitely tender, bluish swelling of the left labia. Directly thereafter, a spontaneous rupture of this hematoma occurred through the medial portion of the labia majora. Profuse, bright red hemorrhage occurred. Immediate measures were instituted to combat the hemorrhage and shock including a blood transfusion and analgesic medication. Consultation was held immediately with four other staff general physicians, two of whom perform major surgery routinely.

The physical examination revealed a well developed, well nourished, white female in actute distress with pain in the perineum and a bulging blue left labia majora. Blood pressure was 95/60; pulse 120. Skin was markedly pale and sallow. Patient was listless and exhausted. Eyes, ears, nose and throat were not remarkable. The neck was negative except for slight enlargement of the thyroid. The chest showed no abnormality; the heart and lungs were normal. The abdomen showed the usual 36 week ovoid uterus, not undergoing any contractions, and not unusually tense. The liver was not enlarged. Marked tenderness was present throughout the lower abdomen over the bladder and in both adnexal regions. The perineum showed gross bright red hemorrhage from at least two apertures on the medial surface of the left labia majora. The skin over the left labia was tremendously stretched and bluish in discoloration, and beneath it extended a large, soft mass fluctuant in nature from the pubis to the perirectal tissue on the left. This area was exquisitely tender to touch. The extremities were apparently normal and no evidence of varicosities or edema was present.

The operative findings were as follows: An incision was made into the left vulva where many clots were evacuated and no single definite bleeding points were recognizable. Through and through mattress sutures were placed in the area of this massive hematoma and then a snug vaginal pack was inserted. Thereupon, because of the embarrassment of the fetal heart tones, the abdoment was prepared immediately

and a routine Caesarian section was performed. The pelvis was inspected carefully but there was no evidence of any active hemorrhage in either broad ligament or as far as could be seen in the retro-peritoneal spaces. The baby was dead upon delivery and weighed 4 pounds and 1-½ ounces. The anesthetic by choice was a combination of nitrous oxide cyclopropane and oxygen. The immediate post-operative condition was poor. Supportive therapy was continued but post-operative course was rapidly downhill. The patient never recuperated from her shock, in spite of four transfusions and she died 20 hours after admission.

A post mortem examination was done and revealed a large retroperitoneal extension of recent hemorrhage back of the bladder and uterus up along the left ureter and half way to the kidney. Microscopic examination of sections from the liver, spleen and kidney revealed no significant abnormalities.

INCIDENCE

The American literature is comparatively barren of information on this subject. No report of a case of hematoma of the vulva occuring before labor could be found in a brief resumé of recent literature up to 1953. DeLee[3] stated that hematomas of all types occur in approximately one in four thousand labors, and that "in a total pathologic work of over 70,000 routine cases, only 7 cases of large hematomas came under our notice". Lubin and Horowitz[4] in a discussion of post partum hematomas state that *"rarely* the blood mass may appear late in pregnancy". Hamilton[5] in a review of the literature in 1940 found a total of only one hundred fifty-six reported cases of post-partum labial and para-vaginal hematomas. Crossen[6] states it is a rare occurrence to find a case of a hematoma of the vulva in advanced pregnancy or labor in which the swelling may burst and result in fatal external hemorrhage or of a patient bleeding to death without an external opening being evident. Williams found such tumefactions to occur one in fifteen hundred to two thousand cases. In 1904, in 31 cases of sub-peritoneal hematoma which he collected, the mortality was 56%. It is interesting to note that more than 60% of the cases occurred in primipara and 71% after spontaneous labor. It is seen that the report of cases occurring previous to labor is remarkably infrequent.

LOCATION

Davis states that "generally the site of the effusion is the lower vagina or the vulva or both. The swelling usually encroaches upon the vagina and the rectum. Rarely the ruptured vessel is above the deep pelvic fascia, the effusion occurring largely in the subperitoneal tissues. In these latter rare cases, the swelling may be manifest in the upper vagina, but it is prone to extend far upward beneath the peritoneum, where it may make a palpable abdominal mass above Poupart's ligaments or in the false pelvis. The loss of blood in this type of case may be so great as to prove fatal".

Dr. Lee states that the location may occur "under the skin of the vulva, around the vagina, under the broad ligaments and in the broad ligaments". If it occurs "below the levator ani-muscles and the deep pelvic fascia, it will distend the peritoneum

and dislocate the rectum and anus. If around the vagina, it may cause obstruction to delivery. If at the base of the broad ligament, it may extend up into the false pelvis under Poupart's ligament. If behind the broad ligament it may dissect up to the kidneys retro-peritoneally". Crossen points out that the burrowing of extravasated blood in the loose subcutaneous tissues acts to extend the hemorrhage by rupture of neighboring vessels. This is apparently what may have occurred in the case reported here.

ETIOLOGY

There is considerable difference of opinion as to the theoretical explanations of the factors causing hematoma formation. DeLee believes the first major cause is injury. He describes the trauma of spontaneous labor or use of forceps in delivery as the most frequent cause. The second most frequent cause is pressure necrosis, that is, the prolonged pressure of the presenting part of the fetus on vessels in the neighborhood of the vagina, with consequent production of a necrosis, and further dissolution of tissue. Perhaps this could have been a factor in the case reported herein.

DeLee further believes that varices are not a very substantial etiology. To quote him, he states "Varices are said not to favor hematomas".

In contrast to that, Hamilton quotes Vaux and Bland, who "mention the vascularity of the pelvic tissues at the time of delivery with the occurrence of varicosities of the pudendal veins as an etiological factor". Furthermore, Hamilton states that "in our series there were no varicose veins noted in any of the cases".

Crossen believes that "pregnancy, pelvic tumors and other conditions that increase vascularity of the parts predispose to hematomata. The exciting cause is injury that starts subcutaneous bleeding". He further states, "varicose veins of the vulva only rarely give rise to troublesome symptoms. The danger in these cases is that severe hemorrhage may take place or a large hematoma forms from slight injury or from spontaneous rupture of a varicose vein".

Williams states "the condition usually follows an injury to a blood vessel during the act of labor without laceration of superficial tissues, and may follow spontaneous as well as operative delivery". He too believes that "sloughing of a vessel which had become necrotic as a result of prolonged pressure during labor" may be a cause for hematoma formation.

Davis states that, "it is usually associated with the pre-existing varicosities of local blood vessels. The tumor is very generally due to the injury of a blood vessel during labor, spontaneous or operative without laceration of the superficial tissues."

Lubin and Horowitz believe that toxemia of pregnancy and the consequent blood dyscrasias associated with vitamin deficiencies particularly K, contribute to rupture of vessels in cases of post partum hematoma.

SIGNS AND SYMPTOMS

The first symptom of hematoma of the vulva according to DeLee is — "intense

pain, and intolerable pressure on the rectum and bladder." Davis points out that "the sudden onset of swelling with pain and a feeling of tearing and a tender, soft, fluctuant, purple skin are the earliest symptoms". Williams stated that if the tumor is large, it may cause discomfort by its mere size, but it gives rise to great suffering which becomes more intense the more rapidly it is formed, as a result of the tearing and stretching of the tissues.

The signs are dependent upon the location of the hematoma. If near the surface of the vulva, a sausage-shaped tumefaction may be recognizable. On the other hand, a rectal or vaginal examination may show an encroachment upon the lumen of one or the other of these parts. Later the skin or the vaginal mucous membrane covering the tumor may burst and the patient may bleed to death. However, if external rupture does not take place and if the hematoma burrows a great distance, signs of acute severe anemia may become pronounced before external hemorrhage appears. Furthermore, if the condition extends in a retro-peritoneal fashion, the diffused blood may form a tumor palpable above Poupart's ligament or it may make its way into the iliac fossa and gradually invade the renal region and eventually reach the lower margin of the diaphragm. "Paravaginal hematoma and hemorrhage within the broad ligaments are quite easy to diagnose, as a rule. Retro-peritoneal hemorrhage, progressing more slowly than intraperitoneal hemorrhage, and more inaccessibly situated, is probably the most difficult of all these conditions to diagnose".

TREATMENT

Davis states that "small hematomas should be let alone, while often the larger tumors may be best treated also expectantly. If, however, progressive increase in size and continued bleeding occurs, immediate incision and evacuation of the cavity are indicated. Rare cases of subperitoneal variety may when extensive require laparotomy for access to the bleeding site". Lubin and Horowitz in their post partum cases believe that the mass should be opened widely, preferably through the vaginal mucosa. DeLee simply states that during labor, cervical, vaginal and vulval varicosities requiring quick treatment may be best cared for by suture or firm tamponade. Hamilton in his monumental work on post partum hematomas states that "treatment includes first, earliest possible diagnosis; second, incision, preferably through the vaginal mucosa; third, evacuation of clots; fourth, loose packing of the cavity with tight packing of the vagina; fifth, supportive therapy, directed at overcoming shock".

Crossen states that "the open hemorrhage from the genitals should be stopped by packing, or by sutures, or by forceps or by ligature of bleeding tissue en masse, as indicated by the nature of the hemorrhage. If the swelling may burst and fatal external hemorrhage occur, the affection should be treated by operation".

PROGNOSIS

As has been pointed out, mild cases of small hematoma carry a good prognosis. However, Williams pointed out a 56% mortality in the sub-peritoneal variety. Hamilton states that every obstetrician from time to time has prevented the occurrence of these

hematomas, when commencing to do a perineorrhaphy, by noticing a small hemorrhage in one or the other side which he sutured. It would appear that if this complication is recognized early and actively treated, the mortality rate can be materially improved". He further points out that "another interesting observation is that in our series of cases handled in this manner on subsequent examination, there was practically no residual distortion of tissue and three of this series have subsequently delivered with no pathology referable to their previous complaint".

In summary — this is a review of a case of an uncommon complication of pregnancy — a fatal spontaneous hematoma of the vulva. It was evidently hidden injury to the pelvic structures in an apparently normal, eight month gravid primipara, with sudden massive subcutaneous and retroperitoneal hemorrhage, which could not be controlled.

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COR PULMONALE IN ASSOCIATION WITH RAYNAUD'S DISEASE REPORT OF A CASE WITH SYMPATHECTOMY*

E. E. SCHUMACHER, JR. M.D.

Raynaud's disease has generally been defined as an intermittent spasm of the digital arteries brought on usually by exposure to cold and by emotional stress. However, it is known that the disease is not always limited to the digital arteries; since cases have been reported in which intermittent blindness and transient hemiplegia have occurred; supposedly due to spasm of the retinal and cerebral vessels.

In 1941 Linnethal and Talkov[1] first reported three cases of Raynauds disease associated with diffuse fibrotic lung changes, rapidly developing respiratory difficulties and some degree of right sided heart failure. Unfortunately no post mortem examinations were obtained. In 1942 Linnethal[2] reported two additional cases with a post mortem examination in one case which revealed vascular changes in the lung and secondary associated pulmonary fibrosis.

Aside from these cases the literature is essentially devoid of reports of this syndrome. I would like to report an additional related case. Unfortunately, autopsy findings are again not obtainable; however, the course was so typical and the response to management so unusual that it is felt the situation warrants review.

The patient was a 46 year old white female who had first noted typical symptoms of Raynauds disease seven or eight years prior to her admission to the hospital. Despite routine management with priscoline, avoidance of cold, etc., her difficulty had become progressively severe until, at the time of her admission, gangrene had begun on several digits on both hands. Approximately two years after the onset of her peripheral vascular symptoms she had noted progressive dyspnea which had continued to increase in severity. One year prior to admission, ankle edema had developed and hepatomegaly had been described by her local physician. Her past history was essentially negative although it was interesting to note that previous examinations in earlier years, at various large centers, had revealed no signs of any cardiac pathology or lung disease and routine chest films and electrocardiograms has been normal.

The essential features, upon physical examination in 1956, showed dusky finger tips on both hands, with a markedly increased capillary filling time and areas of necrosis were noted over the terminal phalanges of several digits. The radial pulses were strong; a severe ankle edema was noted bilaterally and the liver was palpable three centimeters below the right costal margin. The cardiac examination was not remarkable, although the pulmonic second sound was greater than the aortic second sound and the left border of cardiac dullness was several centimeters outside the mid-clavicular line. A sinus tachycardia was present and no significant murmurs were noted. The routine laboratory work was normal. An electrocardiogram showed right

*Presented at the Henry Ford Hospital Medical Association June 1st, 1957, Detroit, Michigan.

ventricular hypertrophy without an associated block. The chest films also showed right ventricular enlargement with some slight increase in the vascular markings of the lung. Cardiac fluoroscopy failed to add any new findings and no signs of auricular enlargement could be determined. Routine pulmonary function tests were essentially normal.

The patient was rigorously treated with the usual measures for her peripheral circulatory findings as well as with digitilization, a low sodium regimen and diuretics for her right sided failure. Despite rigid hospital control little improvement was obtained. This necessitated a stellate ganglion block which produced a satisfactory ptosis, miosis and anhydrosis. There was considerable temporary relief from pain in the corresponding extremity and the capillary filling time was markedly reduced. Because of this result a bilateral upper dorsal sympathectomy was carried out with interruption of the rami, ganglia and chains from thoracic one, two, and three. The patient tolerated the operation poorly and developed a shock-like state near the end of the procedure. The patient survived but her situation was critical for several days. No obvious cause for the situation was noted at the time.

Following the sympathectomy her peripheral circulation was markedly improved and a sinus bradycardia replaced the previously noted sinus tachycardia. Inside of a week it became obvious that the signs of right sided failure were decreasing. Edema was much less marked and the liver edge began to recede under the costal margin. A chest film taken four weeks after surgery showed that "the heart is now appreciably smaller than previously noted prior to the operation". Diuretics, etc., were withdrawn but improvement continued despite any significant medication. When the patient was last seen at the hospital, all signs of right ventricular failure were lacking and the extremities were markedly improved with a continued decrease in capillary filling time and lack of duskiness and pain. Unfortunately, the patient died suddenly five months later in her home town during a minor surgical procedure and no autopsy was obtained.

This case is similar to Linnethal's in some respects. The patient started with typical Raynaud's disease which was followed shortly by progressive dyspnea. There were no other logical explanations for the symptoms and finds in either report. The rapid development of difficulty is not typical of any of the usual forms of pulmonary or cardiac disease. This patient differs somewhat from Linnethal's in that the x-rays were not especially suggestive of fibrosis and pulmonary function tests did not support pulmonary pathology.

There is a similarity between this situation and that presented by so called idiopathic primary pulmonary hypertension. In these cases only minimal vascular changes have been noted and it has been therefore postulated that the syndrome results from an increased pulmonary vasoconstriction similar to the essential hypertension in the systemic circulation. The primary objection to this concept has been the supposition that vasomotor control of the pulmonary arterioles is weak and irregular. The vascular lesions in these cases are only intimal thickenings suggestive of arterio-

losclerosis and are considered to be secondary to the pulmonary hypertension. A more severe syndrome had also been observed in which a necrotizing pulmonary arteritis had been seen at autopsy in association with right ventricular hypertrophy of unknown etiology. This situation has been considered analogous to the malignant hypertension of the systemic circulation. Sudden unexplained deaths and intolerance of minor surgical procedures have been reported as typical of these cases. The severe shock and the rapid death of the patient discussed would be compatible with these observations.

From the preceeding discussion I believe we have established some basis for the relief of symptomatology noted by the patient in this case. It would seem reasonable to suggest that further attempts at such surgery might be attempted in cases of primary pulmonary hypertension in an effort to eliminate the reduction in number and caliber of the pulmonary capillaries and arterioles.

In summary, an unusual form of cor pulmonale in assiciation with Raynauds disease has been reported and the dramatic and unexpected response to sympathectomy has been discussed. It would be hoped that a similar surgical approach will be evaluated in the future in the management of allied syndromes.

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URINARY FLUORIDE AND CALCIUM EXECRETION IN PERSONS SUSPECTED OF FLUORIDE INTOLERANCE*

G. L. WALDBOTT, M.D.

Certain individuals ingesting minute quantities of fluoride in either food or water are unusually susceptible to ill effect[1,2,3]. Because of the sparsity of objective laboratory data in chronic fluorosis[4] a clinical test to determine an individual's tolerance to fluoride would be of great value. In an effort to establish such a test urinary excretion studies were undertaken. Whereas no answer can be given as to the validity of this test at this time, other data were sufficiently conclusive to warrant reporting.

FLUORIDE AND CALCIUM

The literature indicates that the tendency for fluorides to accumulate in the system varies greatly from person to person[5,6]. There is ample evidence that fluoride affects the calcium metabolism in the system: In acute fluoride intoxication blood calcium levels were noted as low as 2.6 mg%[7] and 5.6 mg%[8]. Leone, Geever and Moran[9] noted blood calcium levels as low as 6.5 mg. during acute experimental intoxication by the oral and intravenous route.

In chronic protracted intoxication, on the other hand a disturbance, but not necessarily a decrease in calcium in the blood, is apparent. DeSenarclens[10] reported blood calcium levels as high as 14.5 mg% in protracted experimental intoxication.

In animals grazing near factories emanating fluoride[11], in men suffering from industrial poisoning[4] and from drinking fluoridated water[12], the clinical manifestations and laboratory findings of chronic fluorosis coincide markedly with those of hyperparathyroidism. Certain urinary, gastro intestinal and central nervous system manifestations, as well as bone changes characterized by demineralization, are encountered in both diseases. In my own cases of fluorosis a slight but definite increase in blood calcium levels was noted. In contrast to hyperparathyroidism, however, serum phosphorus levels were usually elevated. A disturbance of the calcium metabolism, due to fluoride's strong affinity for calcium, has been suggested by many authors.

In an attempt to establish a test for detection of intolerance to fluoride, it seemed desirable to determine whether or not a coordination exists between excretion of fluoride and that of calcium. A perusal of the literature indicates that no such studies have been made.

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A fluoride tolerance test must take into account the many variables which influence urinary excretion of both calcium and fluoride; the test must be safe and practicable, in other words it should not require too complicated an apparatus and it should be inexpensive.

Fluoride Excretion: It has been demonstrated[12] that the largest portion of a given dose of fluoride is excreted in the urine; a small fraction (less than 10%) through the bowels, the salivary and sweat glands[14]. Under certain conditions more fluoride is stored in the system, whereas at other times more is liberated and excreted[15]. The presence of calcium in food and water interferes with fluoride absorption into the blood stream[16]. There is a tendency for the body to establish an equilibrium between fluoride intake and output yet, after prolonged ingestion fluoride metabolism may remain in a negative balance for months and even years[17,18].

For practical purposes a test pertaining to excretion of fluorides should not extend over a period of more than 2 days. In administering a standard diet preceding the test, we must take into consideration the fact that the fluoride content of some foods, especially certain vegetables, may vary considerably depending upon where they are grown[19] and processed. Therefore, the test dose of fluoride to be ingested must be large enough to overcome such minor variations in fluoride intake; it must be small enough not to induce ill effect.

Calcium Excretion: Calcium excretion in the urine depends largely upon the daily calcium intake. The patient must therefore be placed on a standard calcium intake for at least 3 days. A low calcium diet containing 137 mg. (Albright[20]) was chosen for the test.

A more exact method of carrying out the test would comprise simultaneous determinations of fluoride and calcium in faeces, sweat and salvia. However, fluoride excretion through channels other than urine constitutes only a small fraction of the total fluoride output. Furthermore, such determinations would not be suitable as a practical clinical test. As to calcium, we are less concerned here with its total output than with its relation to fluoride elimination in the urine.

Some fluoride preparations such as calcium fluoride and calcium fluosilicate are not as readily absorbed from the gastro-intestinal tract as sodium fluoride. Sodium fluoride, therefore, was selected as the compound of choice.

METHOD

After several modifications the following technique was adopted:

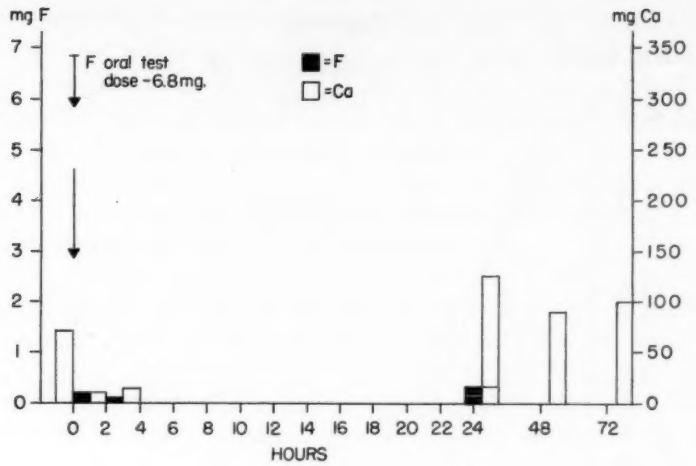

Chart 1

Three Day Course of Fluoride and Calcium Excretion following a test dose of Calcium Fluoride in a Patient with tooth decay. Twenty-four Hour Excretion of F = 4.7% of the Test Dose.

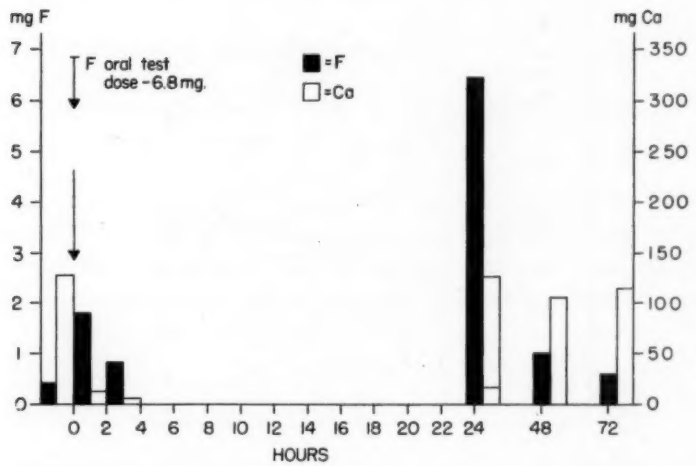

Chart 2

Three Day Course of Fluoride and Calcium Excretion Following a Test Dose of Calcium Fluoride in a Patient with Rheumatoid Arthritis. Twenty-four Hour Excretion of F = 92% of Test Dose.

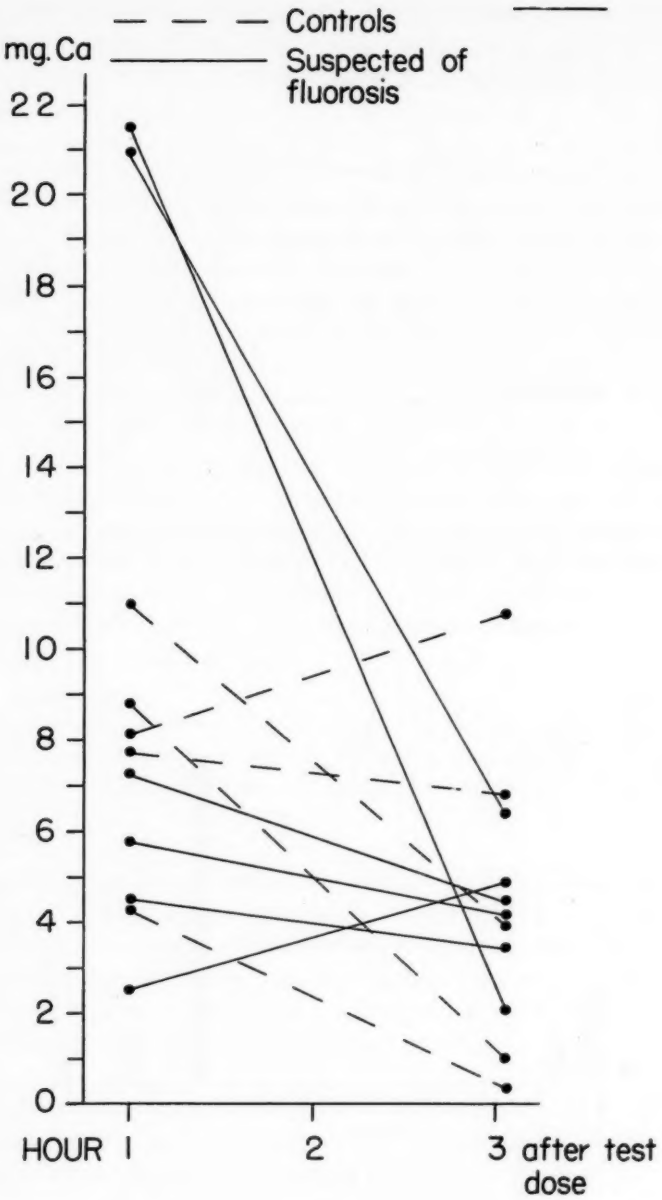

Chart 3

Urinary Calcium Excretion during first hours after Fluoride test dose. Eleven cases.

The Albright diet is administered for three days prior to and during the test. On the fourth day the 24 hour specimen of urine is collected for baseline determinations of calcium and fluoride; 15 mg. of Na F (6.8 mg. F) is when administered on a fasting stomach in 400 c.c. of water in two portions, 15 minutes apart. Urine collections are made after 1-1/2 hours, 3 hours, 24 and 48 hours.

The urine is collected in a glass or plastic container with a plastic top. Contact with metal may interfere with the correct determination.*

Dividing the test dose into two portions of 7-1/2 mg each is a precautionary measure to detect any outward symptoms before administering the total dose.

As much as 6.8 mgm of F is given in order to counter minor analytical errors which might be encountered in the small sized specimens collected during the first 3 hours.

The following data were charted: (Charts 1 and 2).

a) The total baseline urinary fluoride and calcium output on the day before the test.

b) The amount of the two collections within the first three hours.

c) The total 24 and 48 hour urinary fluoride and calcium excretion.

d) The proportion of urinary calcium to fluoride excretion initially, within the first 3 hours and during the total test period.

Among 13 patients (Table 1) seven had suggestive symptoms of fluorosis, six were controls. Two of the seven had minor ill effects and two a more sustained recurrence of former symptoms of fluorosis following the tests. None of the three others and none of the controls had any discomfort whatsoever following the test dose.

RESULTS

The following results can be recorded so far:

1. There were great individual variations in total fluoride output during the 24 hours. The lowest 24 hour excretion was 4.7%; the highest 99% of the 6.8 mg test dose.

*Fluoride determinations were made according to Official Methods of Analysis of the Association of Official Agricultural Chemists; Eighth Edition, 1955, P.O. 540, Benjamin Franklin Station, Washington 4, D.C.

Table 1

Urinary Fluoride and Calcium after the Oral Fluoride test in thirteen patients.

Case	Symptoms Suggestive of Fluorosis	Volume	24 Hour Urinary Excretion F in Mg	% of Total Intake	Ca Mg
° 1. Mrs. E. S. 58	G. I. and Neurological	1965	2.23	33%	133.4
° 2. Mrs. M. J. 37	G. I. Neurological, Stomatitis Migraine	3665	2.71	40%	160
° 3. Mr. R. R.* 43	Joint Swellings	1747	3.80	56%	480
° 4. Mr. F. L. P. 60	Stomatitis, Migraine and Joint Swelling	1870	1.17	16%	79
5. Mrs. D. M. 25	Urinary and Joint Symptoms	3000	3.24	48%	41
6. Mrs. A. L. 46	Urinary and Joint Swellings	1407	.52	7.6%	114.7
7. J. M. 7	Mottled Teeth	1621	.77	11%	111.4
			av. = 2.06		
Controls	Diagnosis				
° 8. Mr. L. L. 33	Psoriasis	1935	6.77	99%	360.1
° 9. Mrs. R. B. 61	Gastro-intestinal Allergy	3272	3.56	52%	178
°10. Mrs. T. W. 43	Arthritis, Respiratory Allergy	680	2.17	32%	101.5
11. Mr. A. J. B. 60	Rheumatoid Arthritis	1929	6.23	92%	134.8
12. D. K. 11	Rapid Tooth Decay, Respir. Allergy	1680	.321	4.7%	128.7
13. Mrs. I.K. 41	Urticaria	1040	.610	9%	41.8
			av. = 3.27		

*Urinary Ca excretion closely paralleled F. output in this patient.

°These cases were on a regular diet previous to test.

Table 2

Serum Calcium, Phosphorus and Alkaline Phosphatase
Values following Ingestion of 15 mg Na F (6.8 mg F)

Name - Age	J. S.* 35		S. C.* 8		M. N.* 50		M. D.* 57		W. H.* 16		K. K. 13		I. K.		J. C. 70	
Diagnosis	Sterility Mottled Teeth		Hearing Defect		Arthritis Migraine		Arthritis Br. Asthma		Tetaniform Convulsions		Stained Teeth		Urticaria		Pruritus Ani	
Blood	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After	Before	2 Hr. After
Calcium	10.2	11	11.2	11.4	10.3	11.3	9.2	10	10.3	10.1	10	10	10.8	10.2	10.3	10.4
Phosphorus	2.9	—	4.4	4.7	3.5	3.9	3.2	4.4	5.4	5	4	4.1	2.6	2.6	2.8	2.9
Alkaline Phosphatase	4.4	6.3	10.5	6	1.5	1.1	4	4	11.3	15.4	6.7	7.7	4.2	4.2	3	4.4

All patients had been on a low calcium diet (137 mg) 3 days prior to test.
*Suspected of Fluoride Intolerance.

2. In 9 out of 11 cases there was an initial drop in calcium excretion during the first 3 hours (Chart 3). During this time between 5.3% and 35.3% of the total 24 hour urinary F output was eliminated.

3. The total 24 hour urine output ranged from 680 cc to 3665 cc.

COMMENT

Whereas in most of seven patients suspected of fluoride intoxication the 24 hour urinary fluoride output was low, (average 2.06 mg, extremes 3.80 mg and .52 mg) it is still too early to decide whether or not this procedure will meet the requirements of a clinical test. Great variations in the excretion curves were noted in the 6 control cases without previous evidence of intoxication (average 3.27 mg; extremes 6.77 mg and .32 mg) as well as in those afflicted. Fluoride excretion and fluoride storage may not necessarily parallel the production of symptoms and their severity. In some individuals even minute doses of fluoride might affect certain body structures merely by virtue of "streaming through," rather than due to accumulation in these structures.

Whether decreased fluoride output in some individuals indicates that less fluoride was absorbed into the blood stream or that more fluoride was stored in the system must await further exploration.

If the urinary fluoride and calcium excretion parallels the production of symptoms, this test will serve as a tool for additional studies on fluoride excretion as well as for other types of clinical investigation. It could be employed especially in cases with vague gastro-intestinal symptoms, (gastrititis, colitis, stomatitis), in nephrolithiasis and pyelitis, in arthritis, especially of the lower spine and in migraine like headaches of unexplained origin.

In 8 cases blood calcium, phosphorus and alkaline phosphatase levels were determined within 1-1/2 hours after the test dose. Whereas this study is still incomplete there is a definite tendency to a rise in calcium and phosphorus values as indicated in Table 2, both in cases suspected of fluorosis and the controls. In some, blood phosphorus levels increased simultaneously with the blood calcium.

8 cases suspected of incipient fluorosis and 6 controls were given orally 15 mg of Na F (6.8 mg of F). Fractional fluoride and calcium determinations in the urine were made after 1-1/2, 3 and 24 hours.

The 24 hour fluoride excretion ranged widely from 4.6% to 99% of the test dose; the total urinary volume from 680 cc to 3665 cc.

In 9 out of 11 cases there was an initial decrease of urinary calcium output within the first 3 hours.

Further studies are in progress to determine whether or not this test can be utilized as a tool for detection of intolerance to fluorides.

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ONE-DROP TEST FOR URINE PROTEIN DETERMINATION

EDWIN M. KNIGHTS, JR. M.D. AND JOSEPH C. ERWIN, M.D.*

Although tests for proteinuria have been a fundamental part of laboratory urinalysis for over one hundred years, most of the technics currently employed are still based on the original precipitation phenomeon principle which was originally employed. Recently a new colorimetric tablet test has been devised for the detection of protein in urine. This test is called Albutest† and is supplied as soft tablets along with color chart and directions.

To perform a test, a drop of urine is placed on the tablet followed by two drops of water. An immediate color development takes place if protein is present, and the surface of the tablet is then compared with a color chart to establish the extent of the reaction. If there is no protein in the urine, the tablet will remain yellow, whereas in the presence of protein a blue-green spot will persist on the tablet. Increased amounts of protein influence the intensity of the blue-green reaction.

The Albutest tablet contains cellulose which absorbs on the surface of the tablet any protein in the urine. The color reaction is obtained by means of the indicator bromphenol blue, and a salicylate buffer is also present. The function of the buffer is to provide in the moistened tablet a reaction which will maintain the yellow color of the indicator.

In the presence of protein, the indicator exhibits the "protein error of indicators" first described by Sorenson in 1909.[1] This effect, which has been an obstacle for many years to biochemists attempting to use indicators to measure pH of body fluid, has been studied quite extensively in urine and body fluids. Exton[2] devised a colorimetric test for albuminuria in 1925 using sulfosalicylic acid and the indicator bromphenol blue. Qualitative tests for proteins have been devised by Feigl and Anger[3], by Ishidate and Sakaguchi[4], Joukovsky and Vandervelden[5], and Ketomaa and Ruosteenoja[6]. Many ph indicators have been found to be affected in this manner and the ethyl ester of tetrobromphenolphthalein has been found particularly desirable for serum protein methods. Klotz found that albumin was quite unique in its affinity for small anions[7,8], and in 1953 Bracken and Klotz reported a simple method for rapid determination of serum albumin using methyl orange (sodium p-die-methylaminoazobenzene-p'-sulfonate)[9]. With this dye equilibrium between zwitterionic acid form and anionic basic form is at its midpoint near pH 3.5 and upon addition of serum albumin, color shifts markedly towards yellow because the protein combines with anions.

The urine tablet test has been studied extensively in the laboratories of the Department of Pathology of Harper Hospital and compared with sulfosalicylic and Kingsbury-Clark technics[10]. It was found to be a rapid, easy method requiring a minimum amount of urine and no heating. Use of a common drinking straw for transfer of the urine allows the complete elimination of glassware from the procedure, making it an attractive procedure for routine scanning of large numbers of urine

*Department of Pathology, Harper Hospital. Presented by title at the Henry Ford Hospital Medical Association, June 1st, 1957, Detroit, Michigan.

†Albutest is a registered trademark of Ames Co., Inc. Elkhart, Indiana.

specimens either in the office or in the hospital laboratory. Ability of technologists and physicians to interpret the roughly quantitative yellow to blue color change was found to improve considerably with experience. When used by an experienced person, the tablet proved very reliable in picking up human albumin concentrations of 20 mg./100 ml. or greater in more than 2000 urine specimens studied. False positive tests for albumin were infrequent; differences of reaction between the sulfosalicylic acid test and the colorimetric tablet test occurred less than 1% of the time. A decomposed, strongly ammoniacal urine will give a false positive reaction because bromphenol blue is also an indicator on the alkaline side. Tablets appear to be stable at room temperature for at least 5 months. Table I shows the results of examinations of 180 coded urine specimens by 18 persons participating in a recent workshop in ultramicro methods. Human albumin was added in varying concentrations to urine specimens testing negatively by the sulfosalicylic acid technic. No false positive tests were recorded in this group and interpretations were remarkably accurate. An additional set of 18 urines, which have been allowed to decompose and become ammoniacal, gave the following results: test called questionable by five examiners, recorded as negative by eight, 1 plus by two, 2 plus by one, and 3 plus by two examiners.

Table I

Urine Protein Test Results

180 Coded Specimens
18 Examiners

Human Albumin Content (mg. %)	Interpretations				
	0	1+	2+	3+	Totals
500		1	1	16	18
400		1	3	14	18
250		1	4	13	18
120		6	7	5	18
100		2	10	6	18
80		8	9	1	18
50	2	12	3	1	18
20	7	10	1		18
0	36				36

SUMMARY

Evaluation of a new tablet test for albuminuria (Albutest) reveals the test to be a rapid, efficient method of qualitative screening for albuminuria requiring neither heat nor glassware. Previous studies showed roughly quantitative results to agree well with sulfosalicylic acid Kingsbury-Clark methods when albumin was present in concentrations above 20 mg./100 ml. Tablets appear to be stable at room temperature for at least 5 months.

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HERNIATION THROUGH THE DIAPHRAGM INTO THE PERICARDIUM*

J. Forbes Rogers, M.D., Warren Zeph Lane, M.D. and Raymond Gibbs, M.D.

Herniation through the diaphragm has been well documented in the literature and it has been established that various congenital anomalies of the diaphragm represent the basis for the vast majority of non-traumatic herniation. The usual text books of surgery, as well as articles on this subject, list the types of congenital diaphragmatic hernia with which we are all familiar, namely (a) through the hiatus pleuroperitonalis foramen of Bochdalek, (b) through the dome of the diaphragm due to partial absence of the posterior portion of the muscle, (c) through the esophageal hiatus, and (d) through the foramen of Morgagni.

That herniation can occur through the middle leaflet of the central tendon with direct entrance into the pericardial sac has been rarely described. Indeed its occurrence is so unusual that it has not been included in the usual discussions on diaphragmatic hernia.

In 1948 Harrington[1] reported on his extensive personal experience with 400 cases of diaphragmatic hernia, not one of which included a defect in the pericardial sac. A collection of 821 cases reviewed by Hedbloom[2] in 1934 made no reference of herniation into the pericardial sac.

The Library of the American Medical Association has reports of eleven cases in the world literature. Of these, eight were autopsy findings of stillbirths or neonatal deaths in whom defects between the pericardial sac and diaphragm were associated with other anomalies of such magnitude as to be incompatible with life. The remaining three cases[3,4,5] were successfully corrected surgically. Two of these were congenital defects in infants and one was a 48 year old African native with a history of trauma.

The case which we wish to present is that of a 53 year old woman who was admitted to the Stamford Hospital emergency room following an automobile accident. Besides the initial shock, which was promptly corrected, the injuries sustained consisted of compound comminuted fractures of the right tibia and fibula, comminuted fracture of the left radius and ulna, fractured 4th, 5th, and 6th ribs on the right, and multiple abrasions and contusions. An abdominal examination revealed no signs of internal injury and the lungs were clear and fully expanded. She was taken to the operating room where an open reduction of the compound fracture of the tibia was performed and the fractured radius and ulna were reduced. The patient remained in the hospital for a period of eight months during which time her entire care was orthopedic. Approximately one month after admission a chest film indicated a small pleural effusion on the left but was otherwise negative.

Thirteen months after the accident the patient was readmitted because of persistent post-prandial epigastric pain which radiated upward into the left chest. She reported that something seemed to "flop over" when she turned on her left side in bed.

*Given at the Henry Ford Hospital Medical Association, June 1st, 1957 at Detroit, Michigan.

A chest film showed a large bizarre shadow filling the base of the left chest and containing fluid levels. The barium studies of the stomach, small and large bowel indicated that almost the entire stomach and a considerable portion of the transverse colon were in the left chest.

Figure 7

Preoperative x-ray of chest showing radiolucent shadows above the left diaphragm.

Figure 8

Preoperative barium enema.

With a preoperative diagnosis of a traumatic diaphragmatic hernia the patient was taken to the operating room and the left chest was opened through the bed of the 8th rib. To our astonishment the left pleural cavity was normal, and the diaphragm

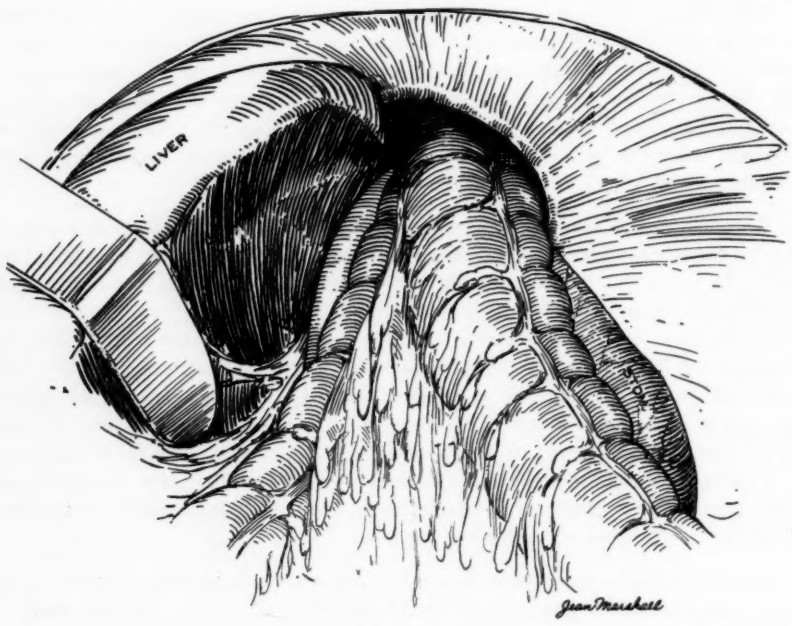

Figure 1

Defect in the diaphragm containing the herniated stomach and colon.

on this side was free of any defect; however, the pericardial sac was distended and upon palpation the presence of bowel could be detected within it. We therefore extended our incision across the costal margin into the abdomen. The true nature of our problem was then apparent. A large round hole was present in the central leaflet of the diaphragm measuring about 8 cm. in diameter with the left lobe of the liver entering it on its right side and with the stomach and colon filling the remainder of the defect (Fig. I). There were no adhesions and no peritoneal sac. When the contents were reduced the heart was freely pulsating against the surface of the liver. The pericardium was smoothly continuous with the peritoneum (Fig. 2). A remarkable finding was the absence of a triangular ligament leaving the left lobe of the liver unsupported. Thus, this portion of the liver could be deflected into the opening. We elected to bridge this defect with a fascia lata graft which was readily done and when completed the liver assumed a position entirely covering the graft and conveniently served to buttress it. The patient's postoperative course was uneventful and at the present time — one year later — there is no evidence of recurrence.

Figure 2

Defect as seen after removing herniated viscera showing peritoneopericardial communication and exposed heart.

To explain this hernia entirely on trauma leaves much to be desired. The smooth continuity between pericardium and peritoneum, the absence of adhesions, and the undeveloped triangular ligament argue strongly for a congenital anomaly. Yet it is difficult to understand how such a defect could persist for 53 years without producing

symptoms. However, O'Brien[6] reports that during dissection of a 63 year old cadaver a similar defect was found in the central leaflet of the diaphragm. The abdominal viscera were prevented from entering the pericardium by the blockade produced by the left lobe of the liver.

A review of the embryological development of the diaphragm will explain the probable origin of this defect, illustrated in Fig. 3 to 6. The middle leaflet of the

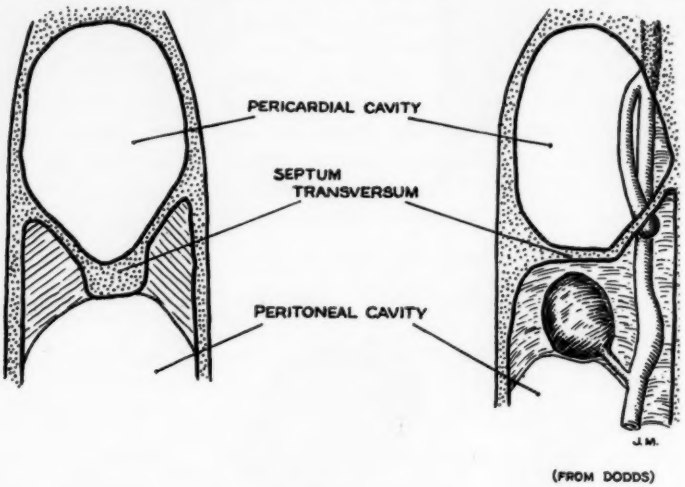

Figure 3

Upper peritoneal cavity (Coelomic Cavity) with pleural recess (shaded area) before development of pleuroperitoneal membrane.

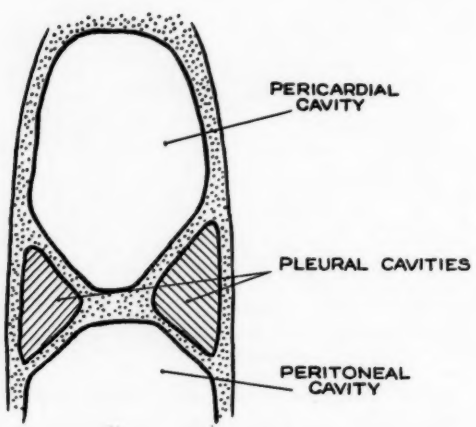

Figure 4

Pleural cavities separated from peritoneal cavities by pleuroperitoneal membrane.

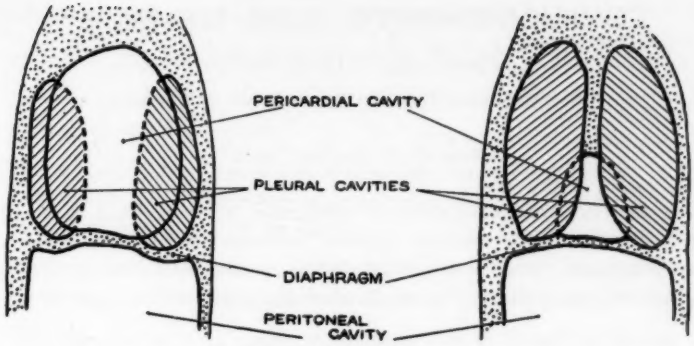

Figure 5 and Figure 6

Pericardial cavity decreases in size with enlarging pleural cavities but retains its relation to middle leaflet of diaphragm (former septum transversum).

central tendon of the diaphragm is formed from the transverse septum which early in development extends across the coelomic cavity. It is this structure which descends from the level of the 4th cervical myotome that carries with it the cervical nerve innervation to the diaphragm. The coelomic cavity above this septum remains as the pericardial sac after the pleural cavities expand on either side with their growing lungs. Fusing with the transverse septum is the pleuroperitoneal membrane which proceeds from the lateral wall. It is a double layered serous membrane, being pleura above and peritoneum below and between which the striated muscle extends to the central tendon. Therefore a defect in this transverse septum or future central tendon will be distinctly different from failure of some portion of the pleuraperitoneal membrane. The former will necessitate a defect into the cephalic coelomic cavity or future pericardium. The latter defect would be through the muscular diaphragm into the pleural cavity.

It is suggested that this case represents a very unusual defect in the diaphragm due to failure of the developing transverse septum to separate the two portions of the coelomic cavity. The congenital basis for the defect is supported by the failure to find evidence of trauma at surgery plus the absence of a triangular ligament. Nevertheless, the relationship of trauma cannot be denied and must be assumed to be responsible for forcing the bowel into a preexisting defect.

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COMPLICATED PEPTIC ULCER TREATED BY COBALT-60* TELETHERAPY

A Preliminary Report of Results in 34 Patients

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During the last three years, cobalt-60 teletherapy has been used at the Cleveland Clinic in conjunction with intensive medical treatment in 34 patients having complicated peptic ulcer. Since a long-term follow-up always is necessary to evaluate properly any new type of therapy for peptic ulcer, this paper is only a preliminary report.

The use of irradiation in the treatment of peptic ulcer is not new, and various technics have been employed to deliver the irradiation to the stomach itself. Previously, we have treated a few patients with a 250-kv. roentgen ray machine. Irradiation by means of cobalt-60 teletherapy unit[1], as we have used it, has been an adjunct to conventional therapy[2] and has not replaced diet, sedation, antacids, and anticholinergic drugs.

The goal of irradiation of the stomach is to decrease acid secretion. Numerous studies have shown that roentgen irradiation at least temporarily decreases gastric acid secretion and frequently results in anacidity[3]. Roentgen therapy for peptic ulcer was first used by Bruegel[4] in 1917 and since has been used by a number of workers. Palmer, Kirsner, and their group at The University of Chicago have employed this form of therapy more extensively than any other group[5-7]. Levin, Clayman, and Palmer[8] reported the results in 723 patients treated from 1937 to 1950 and followed to January of 1956. The recurrence rate of symptoms per 100 patients' years was 102 before treatment and was 17 after treatment. The recurrence rate of hemorrhage was reduced from 4.3 before to 1.1 patient years after treatment and perforation from 0.2 before to 0.1 after treatment. They noted no serious side effects of irradiation. Some patients had erythema of the skin and subsequent tanning, but none developed leukemia. Their study with its long follow-up indicates that the results from the combined use of irradiation and rather strict medical treatment are excellent.

Various technics of irradiation have been used. McGeorge[9] has placed radium needles in the stomach. Brown and associates[10], in England, combined irradiation with antroduodenectomy. Palmer's technic[8] has been to administer 1800 to 2500 roentgen units to the fundus of the stomach through two portals with a 250-kv. machine. The stomach is outlined fluoroscopically before therapy is started. Conventional medical therapy also is given to these patients.

It has been repeatedly stressed "No acid, no ulcer." Any therapy that results in anacidity will be effective ulcer treatment, and even treatment that causes a

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*The radioactive material used in this study was supplied on authorization of the Isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tennessee.

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This study was done with the help and co-operation of Robert A. Hays, M.D., Department of Radiology, The Cleveland Clinic Foundation.

Given in part before the Henry Ford Hospital Medical Association, May 31, 1957, Detroit, Mich.

reduction in acidity may be effective. Previous studies have shown:

1. Irradiation depresses gastric secretion.
2. There is a correlation between the degree of reduction of anacidity and the amount of irradiation given.
3. The decrease in acid secretion may persist for varying periods of time. In a few patients the depression of gastric acid secretion may be permanent but in most patients it is only temporary.
4. While the acid secretion is depressed, particularly if anacidity occurs, the ulcer heals; and the ulcer does not recur until and unless the acid secretion returns.

The technic of irradiation employed in our patients was adapted from that of Palmer,[5,8] except that the cobalt unit was used instead of the roentgen ray machine. While most of Palmer's patients were hospitalized, ours were treated as out-patients. The stomach was outlined by barium fluoroscopically and marked on the skin anteriorly and posteriorly in two fields. These two fields were centered over the upper two thirds of the stomach and were employed for the irradiation. It should be noted that the irradiation is given to the upper two thirds of the stomach, which is the acid-secreting portion, and not to the ulcer itself. Each patients received a total of approximately 2000 roentgen units (depth dose).

The cobalt-60 teletherapy unit has certain physical advantages over the conventional roentgen ray machine. In particular, it has a skin-sparing effect and, being more penetrating, a greater depth dose is obtained. We believe that there is no difference between the biologic reaction to the gamma rays of cobalt-60 and the reaction to the roentgen rays of the 250-kv. roentgen ray machine.

In addition to irradiation the patients were treated medically[2] on an intensive ulcer program. This consisted of a liberal diet, but with food or milk every two hours on the even hours, antacids on the odd hours, mild sedation and anticholinergic drugs.

SELECTION OF PATIENTS

The 34 patients selected for cobalt-60 teletherapy had not responded to previous medical treatment, had evidence of complications or intractability of ulcer and were considered possible candidates for operation. Several had severe cardiac disease contraindicating operation. One patient became cyanotic on the operating table before surgery and operation was cancelled. Cobalt-60 teletherapy was not used in patients having simple uncomplicated ulcers or having a first attack of peptic ulcer.

Of our 34 patients, 28 had duodenal ulcer, four had marginal ulcer, one had gastric ulcer, and one had severe hyperacidity syndrome but no demonstrable ulcer. The average duration of ulcer distress was 11.3 years in the 28 patients having duodenal ulcer. Of these 28 patients, all had had repeated recurrences of ulcer, ten had hemorrhage, six had complications of obstruction, and one had perforation. The average duration of ulcer distress was 11 months in the four patients having marginal ulcer. Two had hemorrhage from the ulcer and all had pain. Two of the four patients

had had two operations each for ulcers. The patient with gastric ulcer had a 15-year history of previous duodenal ulcer. The patient with severe hyperacidity syndrome but no demonstrable ulcer, had been advised by another gastroenterologist to undergo gastric resection because of the severity of the symptoms.

The average length of follow-up in patients with duodenal ulcer was six months (range from 2 months to 2 years). The average duration of follow-up in the other six patients was 11 months. This follow-up is to short for the findings to serve as a basis for final conclusions concerning results of treatment. With a longer follow-up one might expect a return of hyperacidity in more of the patients and a higher incidence of recurrence of peptic ulcer and its complications.

TOLERATION OF THERAPY

As mentioned previously, the 34 patients were given an average depth dose of 2000 roentgen units each, with the cobalt-60 teletherapy unit. Pretreatment and post-treatment white cell counts and hemoglobin determinations showed no significant change. No skin reactions of any kind were observed in any of the patients. Six of the 34 patients complained of nausea and two patients vomited. Cobalt-60 teletherapy was better tolerated than was irradiation with a 250-kv. roentgen ray machine: the same dose delivered with a 250-kv. machine results in some erythema and tanning of the skin and in nausea and vomiting in a higher percentage of patients.

Transient mild jaundice occurred in one patient who had severe cirrhosis with esophageal varices in addition to his peptic ulcer. It was possible that the irradiation resulted in some necrosis of liver cells and jaundice since the patient had very serious impairment of his liver function before irradiation.

RESULTS

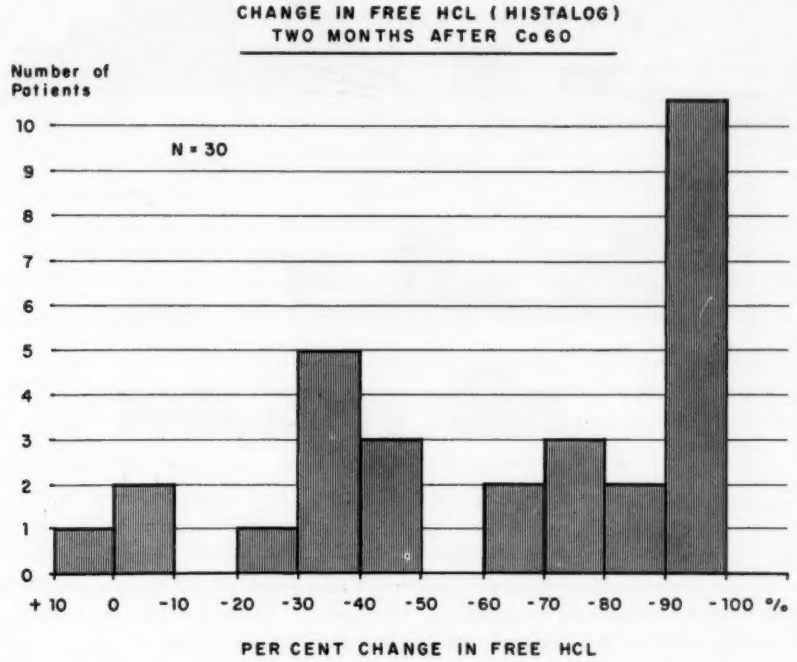
Gastric Secretory Studies

Gastric analysis gives us an objective measure of the effect of irradiation. The possible beneficial effect must be secondary to a decrease in gastric acidity. Gastric analyses with Histalog as a stimulant were obtained before and after irradiation. Histalog, which has been found to be comparable to histamine,[11] was used as a stimulant to obtain a maximum gastric secretory response.

Progress gastric secretory studies were obtained in 2 months in 30 patients. Gastric analyses obtained two months after cobalt-60 teletherapy showed anacidity in seven (23%) of the 30 patients. Eleven (37%) had a reduction in gastric acidity of 90% or more. Eighteen (60%) had a reduction of gastric acid secretion of 60% or more. It should also be noted that 18 (60%) of the patients developed a fasting anacidity which is seldom present in patients with duodenal ulcer.

Six months after treatment with cobalt-60, the depression of gastric acid secretion was not so great. Only 1 in 15 patients had an anacidity to Histalog. Decrease in acidity was less marked in 8 of 15 patients as compared with that two months after irradiation. Consequently, with time there may be a gradual return of gastric acid secretion to pretreatment levels.

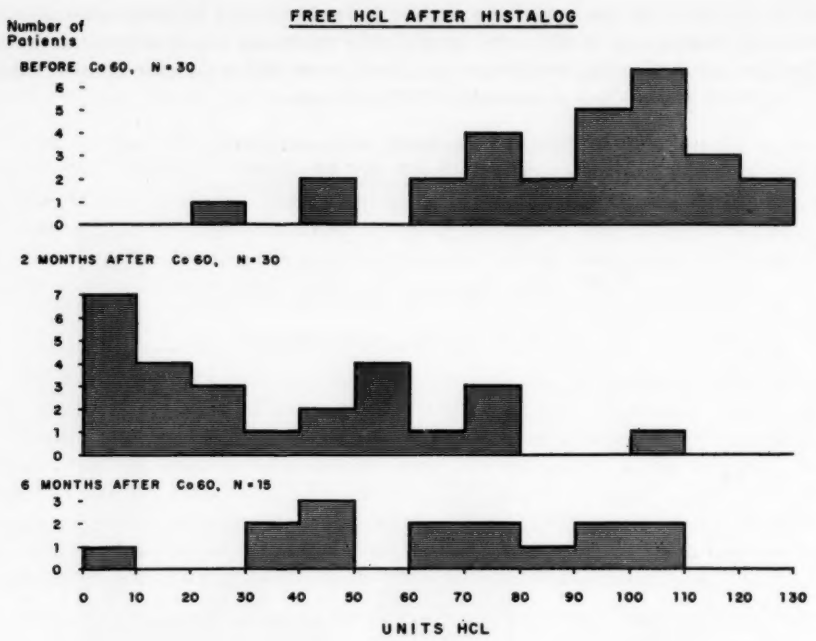
In Figure 1, the per cent change in free hydrochloric acid secretion after stimulation with Histalog two months after irradiation is compared with preirradiation levels. Three patients had no appreciable change; nine patients had a decrease of 20 to 50%; and eighteen patients had a decrease of 60% or more.



In Figure 2 are shown the concentrations of free hydrochloric acid secretion before irradiation, two months after irradiation, and six months after irradiation. In the top graph is a distribution before cobalt-60 therapy. Note the large number of patients with secretion of 90 or more units of free hydrochloric acid. The second curve is a distribution two months after cobalt-60 therapy. Note the marked decrease in acid concentration. The bottom curve shows the acid secretion six months after irradiation. There is a shift of the distribution to levels higher than those found two months postirradiation but still not so high as those found preirradiation. Despite that these studies show that irradiation with cobalt-60 appreciably decreases gastric acid secretion. Such a decrease may be temporary only, at least in some patients.

Symptomatic Response

It is difficult to evaluate symptomatic response of patients having peptic ulcer to any type of therapy. Ulcer is characterized by spontaneous remissions and exacerbations. Nonetheless, the long histories of ulcer in the group, the number of complications and the lack of response to previous medical, and in four cases surgical, treatment are in some measure a control.


FREE HCL AFTER HISTALOG
Number of Patients
BEFORE Co 60, N = 30
2 MONTHS AFTER Co 60, N = 30
6 MONTHS AFTER Co 60, N = 15
0 10 20 30 40 50 60 70 80 90 100 110 120 130
UNITS HCL

Of the 28 patients with duodenal ulcer, 27 had prompt relief of symptoms. One patient had recurrence of symptoms in 12 months. Another patient had an acute perforation in three and one-half months; however, the depression of gastric acidity after cobalt-60 therapy was not great in this patient. Before the perforation occurred, he was entirely asymptomatic and roentgen studies of the stomach showed that the ulcer crater had healed. At operation he was found to have a perforation of a new acute ulcer rather than of the old ulcer.

All of the patients with marginal ulcer obtained symptomatic relief after cobalt-60 therapy, but one year after treatment one patient had a recurrence with a further episode of bleeding. Gastric acidity at the time of the recurrence showed that the hyperacidity had returned.

The patient with gastric ulcer had prompt relief of symptoms; there has been no recurrence during the past 12 months. The patient with the hyperacidity syndrome obtained only partial relief after irradiation.

Roentgen Response

Initial roentgen studies of the stomach demonstrated an ulcer crater in each of the 28 patients with duodenal ulcer. We did not give cobalt-60 therapy unless the patient had a definite ulcer that was demonstrated on roentgenograms. Progress roentgen examinations of the stomach two months after cobalt-60 therapy were obtained in 24 of the 28 patients with duodenal ulcer. The ulcer crater had dis-

appeared in all 24 of the patients, and in addition six patients who showed evidence of obstruction prior to cobalt-60 therapy had no evidence of obstruction on the progress roentgenograms.

In the four patients with marginal ulcer, progress roentgen studies showed the ulcer to have healed in three patients but to have recurred in one.

In the patient with gastric ulcer, progress roentgenograms two months after cobalt-60 therapy showed that the ulcer was healed. For one year since that time, progress roentgen studies at three-month intervals have shown no recurrence of the ulcer.

Failures in Treatment

Failures in treatment occasionally can be more informative than successes. Since the purpose of cobalt-60 teletherapy is to decrease gastric acid secretion, if such a reduction does not occur the case must be listed as a failure. Similarly, if the gastric secretion returns to pre-treatment levels, the case also must be listed as a failure.

Of the 34 patients treated with cobalt-60 teletherapy, nine must be designated as failing to respond satisfactorily. Of these nine failures, six remained asymptomatic but either had a persistence of hyperacidity by gastric analysis or had a recurrence of hyperacidity after an initial depression.

Only three patients were clinical failures having recurrence of hyperacidity associated with recurrence of ulcer. The patient with a duodenal ulcer who developed an acute perforation three and one-half months after therapy already has been discussed. The patient with marginal ulcer who developed recurrence of pain and an episode of gastrointestinal bleeding one year after irradiation has been given a second course of cobalt-60 teletherapy and further medical treatment. Before the first course of teletherapy this patient had undergone two operations for peptic ulcer, a gastric resection for duodenal ulcer followed in six months by a vagotomy for marginal ulcer. The third patient who was a symptomatic failure is a patient with duodenal ulcer with obstruction who had recurrence of symptoms and obstruction one year after irradiation. Because of severe coronary heart disease, this patient was not operated upon but was given a second course of irradiation and continued medical treatment.

Even though the follow-up period is short (average six months), the small number of patients (three) who were symptomatic failures is encouraging. The long history of ulcer in this group of patinets, the number of complications and the severity of the patient's distress make the good response of the remaining 31 patients more significant than if the patients had early uncomplicated peptic ulcer. For example, one of our patients had received 50 to 100 mg. of meperidine hydrochloride, three to four times daily, for relief of ulcer symptoms for three years prior to treatment. He has now been followed for ten months since irradiation with cobalt-60 and has not required a single injection of meperidine. A good response to treatment in such a patient with so-called surgical ulcer is more significant than a good response in a patient with an early simple peptic ulcer.

SUMMARY

Cobalt-60 teletherapy was given to 34 patients with complicated peptic ulcer as a supplement to medical treatment. These patients had not previously responded to medical treatment and had an average duration of ulcer distress of 11.3 years.

Therapy was well tolerated; there were minimal reactions with no skin changes or tanning.

In all but three of the 34 patients, gastric acidity was decreased by cobalt-60 therapy. There was a gradual return of acidity in some patients to pretreatment levels in six to twelve months. The initial symptomatic and roentgen response was good in all patients. There was a recurrence of symptoms, hyperacidity, and ulcer in three of the patients, two of whom have been given a second course of irradiation with cobalt-60.

We do not advise irradiation for the simple uncomplicated peptic ulcer that should respond to conventional medical treatment. Irradiation with cobalt-60 may be indicated in many patients with complicated or "surgical" ulcer or with repeated recurrences of peptic ulcer. Surgical treatment may be avoided in some of these patients with complicated peptic ulcer by the combined use of cobalt-60 irradiation and intensive conventional medical therapy.

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SOME PRINCIPLES TO BE CONSIDERED IN THE REHABILITATION OF CLEFT LIP AND CLEFT PALATE CRIPPLES

RAYMOND S. ROSEDALE, M.D.*

The current movement to develop interest in rehabilitation of the crippled child as evidenced by local and national associations for those afflicted with poliomyelitis, cerebral palsy, muscular dystrophy, nephrosis, pancreatic cystic disease, etc. is especially appealing because of the obvious physical deformities and some of the far reaching complications of these diseases in infants and young children. One of the earliest classifications of congenital disease to receive attention in this country is that of children born with cleft lip and/or cleft palate. These children deserve as much attention as those mentioned above, for not only are they crippled, but many times have multiple handicaps. Too often, the attention to them has pivoted about their anatomical defects. This should not be so, for although they are crippled cosmetically, they are often crippled also in speech, dentition, normal facial growth, hearing, social adjustment and, not infrequently, in the development of psychologic trauma. While children with these lip and palate deformities may not so frequently appeal to the emotions, these patients with their multiple handicaps deserve generous attention so that they may reach their most useful place in society.

Since the latter part of the last century, the greatest emphasis in the care of these unfortunate babies has been in the closure of the palate opening, and the closure of the cleft lip. However, there is more to the problem than just the surgical closure and mechanical management of those deformities. Often the surgeon has had to carry the entire responsibility for the care of the cleft cripple and at times, his efforts have been entirely directed to closure of the lip and repeated attempts at closure of the cleft palate. His efforts have been concentrated on shutting off the fistula, so that the glottic blast, instead of being short-circuited through the cleft, would have to traverse the moulds of speech, namely the teeth, tongue and lips. Occasionally, scarred, thickened, short, tight or perforated palates would develop and in time orthodontists and prosthodontists began to take issue with the surgeons as to the most efficient method and proper time for cleft palate closure.

Actually, the mechanical closure of the oronasal fistula is and should be considered the least part of the problem in rehabilitation of cleft children. The principal objectives of restoration should be the restoration of normal speech, the normal growth of the maxilla, proportioning of the face, dentition, preservation of hearing, speech therapy and psychologic adjustment.

The day of the surgeon having to assume total responsibility for the direction of the care of the cleft child is outmoded. For total restoration, a well patterned program can best be accomplished by a group of specialists, which may be designated "the cleft team," (a) Dental specialists, e.g., the orthodonist, prosthodontist and exodontist; (b) Medical specialists, e.g., the pediatrician, otologist and surgeon; (c) Auxillary specialists e.g., child psychologist, audiologist, and speech therapist.

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The objective of the team is to have each patient reach the fullest degree of functional as well as anatomical rehabilitation. The meetings of the team should be held regularly and its patients considered by each of the members and the plan of treatment modified with the progress of the patient. The captaincy of the team should be vested in the individual with the greatest understanding of the problem.

The care of the cleft cripple begins at birth. The parents must be acquainted with the problem and reassured by allowing them to view photographs of restored children. Reassurance as to the improbability of clefts in future siblings should be emphasized. True cleft families are rare.

Realizing that there are two schools of thought in the matter of timing of repair of cleft palates, it is the author's opinion that single cleft lips should be repaired within the first three days of life, provided there is no systemic contraindications. The reasons for this belief are as follows: Newborns are relatively shook-proof; they possess a favorable fluid balance; they have a greater number of red blood cells and amount of hemoglobin than at any subsequent time. Newborns have a relatively great humoral resistance to infection because of their maternal endowment of agglutins, lysins and opsonins. Tissue healing is generally favorable; little anesthesia is required (I prefer intratracheal anesthesia). With an early lip repair, the newborn may return home to its expectant relatives on about the seventh day, thereby relieving emotional tension. Early closure of a single cleft facilitates and speeds the approximation of the palatal processes in those with cleft palate. In doing early repairs of the single cleft lip it is important to avoid "tight" lip and subsequent contractures and collapse of the healed processes with dental and maxilla deformity.

It has been learned by experience that full correction of the nasal deformity should be attempted at the time of the lip repair and also that the correction does not interfere with the growth of the nose.

Double cleft lips are usually not repaired so soon. The tissue is too scant and there is the complicating technical problem of the protruding pre-maxilla. Timing of repair of the cleft palate is variable with the degree and type of the cleft. Surgical closure itself is not the only important thing, but the attainment of good understandable speech, the preservation of hearing and proper growth of the maxilla are also of paramount importance. Many patients, of necessity, have been well rehabilitated with good prosthetic devices. The disadvantages of the permanent prosthesis are obvious, but if complicating deformities follow surgery, protheses may be needed. These are matters for the cleft palate team to decide in the interest of the individual patient.

In this country it is customary in many areas for the surgical closure of the palate to be done at, or shortly after, the age of 17 months. In some areas also, the cleft palate is successfully closed at the age of one year or less. It is the feeling of some that the cleft palate should not have surgical treatment until the age of six to eight years or later. This opinion has a basis in the patients seen with useless palates, in those without intelligible speech, those handicapped by "parrot beak" noses, inadequate dentition and prognathism. The responsibility of the surgeon who operates

at the early age is considerable and he must have a knowledge and skill which will enable him to achieve closure without appreciable deformity.

In those unsuccessful cases where the scarred, useless palate would only be more damaged by further surgery, it is better to open the palate to such a degree that a prosthesis with adequate bulk for velopharyngeal closure can be fitted and retained.

The usual successful results of early, adequate repair are illustrated by the following plates:

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Figure 1a

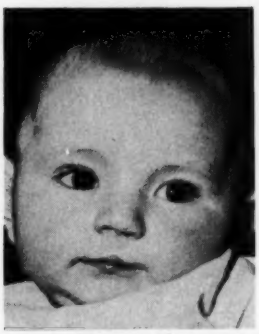

Figure 1b

Fig. 1a. Single complete uni-lateral cleft palate. Age 24 hours. Note repair of nose.

Fig. 1b. Later Gillie's Cupid Bow operation will be done to restore full thickness of vermillion portion of lip which was congenitally deficient.

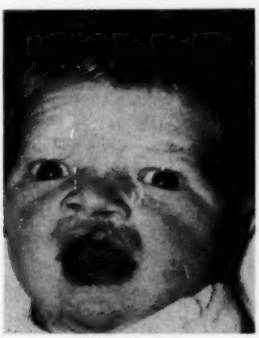

Figure 2a

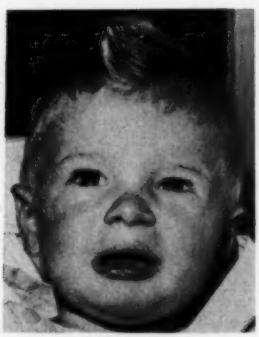

Figure 2b

Fig. 2a. Uni-lateral single incomplete cleft lip repaired at birth.

A—Before

B—After

Figure 3a

Figure 3b

Fig. 3a. Surgical repair of uni-lateral incomplete cleft lip at age 24 hours.

Fig. 3b. Note repair of nose.

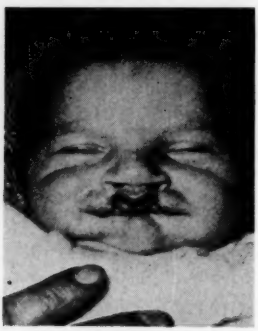

Figure 4a

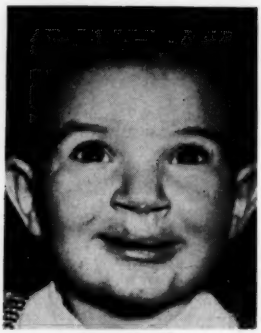

Figure 4b

Fig. 4a. Almost complete double cleft lip. Repair age six weks. Uni-lateral surgical restoration. Opposite side six weeks after first stage.

Fig. 4b. Note full lip, full vermillion and reasonably good restoration of nose. Palate repair done at 17 months.

Figure 5a

Figure 5b

Fig. 5a. Pre and post prosthesis. Previously scarred and short palate precludes adequate surgical management. A dental appliance (prosthesis) to achieve velo-pharyngal closure.

Fig. 5b. View of appliance removed from mouth.

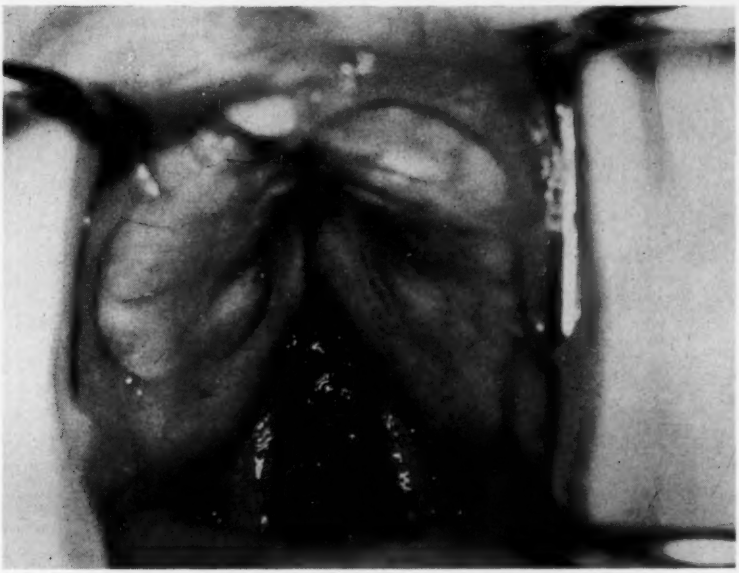

Figure 6a

Fig. 6a. Illustrates closure of palate defect due to physiologic muscle compression following an early closure of the uni-lateral single cleft lip.

Figure 6b

Fig. 6b. In this case, physiological closure of the palate has been too rapid due to tightness of the lip and has been accompanied by some collapsing of palatal arches.

RESPIRATION IN THE NEWBORN INFANT

A. Robert Bauer, M.D.* and Philip J. Howard, M.D.**

During the last 30 years progress has been made in the study of respiration in the newborn infant, both from the standpoint of an understanding of the physiology involved and of the intelligent use of therapeutic measures which have been made available for respiratory difficulties. Since some of the pioneer work in that field was done at this hospital by Howard and myself[1,2,3,4] I would like to briefly summarize some of our results together with those of some other clinics.

Our first work was done with a body plethysmograph in which the infant's entire body was enclosed in a metal tank with the head protruding through a rubber collar similar to a Drinker respirator, allowing the patient to breathe room air. The air displaced inside the tank was equal to the amount of air taken into the respiratory tract, and by connecting a recording spirometer to the inside of the tank we were able to get faithful measurements of rate, tidal air and minute volume, and by placing inflated rubber tubing around the chest and abdomen we were able to get records of these movements at the same time. In another part of this experiment, we obtained tracings while administering varying concentrations of oxygen to the subject and making analyses of the respired mixture at one minute intervals with a Beckman oxygen analyser. As a result of these studies, we were able to show that low oxygen concentrations of 12% or less acted as a respiratory depressant in newborn infants, whereas concentrations of 40% or more were stimulating and resulted in increased minute volume. This was more or less true regardless of the pattern prior to the experiment; that is, if the respirations were regular and efficient in room air, the administration of 12% oxygen would convert them into an irregular inefficient type. On the other hand, if they were irregular and inefficient in room air, the administration of higher concentrations would make them regular and increased the minute volume in 7 out of 10 infants. These results were similar to those previously reported in prematures by Wilson, Long and Howard[5].

The newborn infant's response to oxygen is almost the opposite to that found in adults who respond to low oxygen with hyperpnea and to high oxygen with a reduced respiratory effort. We found that at about 30 days of age the infant began to change over to the adult type of response. We were unable to demonstrate any pattern of coordination between chest and abdominal movements or that such lack of coordination contributed in any way to inefficient breathing. We felt that the breathing was chiefly abdominal and that the chest merely acted as a support for the pull of the diaphragm. At the end of each experiment, we administered 5% carbon dioxide in 95% oxygen and found it to be a most powerful stimulant in increasing minute volume.

Different explanations are offered for the peculiar newborn response. The most popular view at present is that the respiratory center is depressed by anoxia and does

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not respond in its usual way to changes in carbon dioxide tension, and the chemoreceptors situated in the aorta and carotid arteries take over the control of respiration by responding to changes in oxygen tension. This would imply that the inefficient breathing was the cause of the anoxia which had depressed the respiratory center, and that the administration of oxygen relieved the anoxia and returned the center to a normal status so that it again responded to changes in carbon dioxide tension in the usual way. Cross and his associates in England[6] have presented what they feel is very strong evidence to support this view.

Our explanation is somewhat at variance with theirs. We feel that this type of breathing is physiological for the newborn and simply represents his way of quantitating his relative oxygen and carbon dioxide tensions. It has been shown by Wilson and his group[7] that the newborn has a low oxygen saturation and carbon dioxide tension, with a slight uncompensated acidosis which were interpreted to indicate a relatively anaerobic existence. It would seem to follow that if less oxygen were used in oxidative processes, there would be less carbon dioxide formed, since it is one of the end products of oxidation in the tissues. Because of the different solubility, diffusion and mixing characteristics of oxygen and carbon dioxide, shallow, irregular breathing with occasional periods of apnea tend to conserve carbon dioxide without proportionately diminishing oxygen intake. Since the relatively anaerobic existence and peculiar type of fetal hemoglobin offer some protection against anoxia, and the low carbon dioxide tension allows the infant to endure a greater retention of carbon dioxide without toxic effects, it would appear that both are some insurance against a prolonged interruption of oxygen and carbon dioxide exchanges which may occur during delivery or after delivery and before the infant's own respirations have been started.

Winterstein[8] has advanced an interesting idea of respiratory control which he calls the "reaction theory"*. It proposes that all regulation is on the basis of pH change

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*Author's understanding of Winterstein's Reaction Theory:

Winterstein's explanation of how anoxia increases sensitivity of the respiratory center to CO_2 stimulation: Oxygen lack causes hyperpnea which reduces the numerator of the Henderson-Hasselbach equation by washing out CO_2 $cH = K\frac{(H_2CO_3)}{(HCO_3)} = \frac{3}{60} = \frac{1}{20}$. "If the numerator is increased by the addition of carbon dioxide in the inspired air in a proportion of 3:1, the fraction becomes $3+1/60=4/60=1/15$." Now, if because of anoxia, the absolute value of the fraction is reduced, that is, the hyperpnea washes out CO_2 reducing the numerator from 3 to 1 and the denominator is also reduced from 60 to 20 to preserve the 1/20 ratio by the action of kidneys and other buffer mechanisms; then if the same amount of CO_2 is added as mentioned above, the fraction would then be $1+1/20=2/20=1/10$ which will give a lower pH than the 1/15 and hence a greater stimulation. Or stated another way, the same quantity of CO_2 will cause a greater stimulation of respiration in an individual whose absolute value of H_2CO_3/HCO_3 has been reduced by acclimatization to anoxia. These figures were intentionally made simple and exaggerated. He also stated that this could be predicted mathematically from the Henderson ratio, but has also been reproduced experimentally, and that metabolism during anoxia is the same or even greater, producing as much or more CO_2

NH_4Cl put into the blood causes it to shift strongly to the acid side, but the spinal fluid to the alkaline side and the increased ventilation is the algebraic sum of these two actions. This is the opposite to what Gessel found with $NaHCO_3$. The undissociated ammonia molecule (in the blood), appearing from the dissociation of the ammonium ion $NH_4 \rightleftharpoons NH_3 - + H+$, diffuses thru the barrier which is impervious to the ions. On the other side (spinal fluid) it again dissociates $NH_3 + H_2O \rightleftharpoons NH_4 + + OH-$ thus causing the alkalinity in the spinal fluid.

$NaHCO_3$—"The physiochemical process is obviously as follows: In the original solution the equation $CO_3 - \rightleftharpoons CO_2 + + OH-$ gives the solution its alkaline properties. The CO2 wanders thru the membrane to the other side, where it becomes $CO_2 + H_2O \rightleftharpoons HCO_3 - + H+$ thus giving an acid reaction". The reaction $H_2CO_3 \rightleftharpoons CO_2 + H_2O$ is a slow one, but is speeded up with carbonic anhydrase which is present *inside the red blood cells.*

whether in the respiratory center or in the chemoreceptors and also whether thru oxygen or carbon dioxide variation. In the case of carbon dioxide, the effect on the respiratory center can be direct thru the blood or indirect thru the spinal fluid. The amount of carbon dioxide in the blood changes the pH by dissociation of H ions from H_2CO_3, and as the blood bathes the center it is stimulated by these ions. In the spinal fluid these changes are brought about in quite a different way. Since the spinal fluid-blood barrier is impervious to ions, H ions cannot pass thru regardless of origin, but molecules such as carbon dioxide pass thru freely. Once in the spinal fluid the carbon dioxide forms carbonic acid which dissociates into H ions that are able to stimulate the center.

In the case of oxygen, he feels that the lack of it within the center or chemoreceptors gives rise to acid metabolic products which lower the pH and stimulate them from within. Paradoxically, the ensuing hyperpnea washes carbon dioxide out of the blood giving laboratory findings of a respiratory alkalosis at a time when the interior of the centers are in a state of relative acidosis. He also states that anoxia makes the respiratory center more sensitive to stimulation by carbon dioxide and explains it in this way: anoxia causes hyperpnea which washes carbon dioxide out of the blood, thereby reducing the numerator of the Henderson-Hasselbach equation from its usual $1/20\text{-}H_2CO_3/NaHCO_3$, and since the 1/20 ratio must be maintained the denominator is also reduced resulting in a total diminution of both. Consequently, a given quantity of carbon dioxide, either retained or administered will cause a greater increase in the numerator which reduces the pH and stimulates the respiratory center.

Miller and his group in Kansas City[9] have done excellent work in this field and have concluded that the chemoreceptors are less sensitive in the newborn than in later life, in sharp disagreement with the stand taken by Cross and a little more in line with the view which we have taken. They[10] also brought out an interesting point by allowing newborns to breathe a low concentration of oxygen, and then by giving 5% carbon dioxide in that atmosphere of low oxygen they were able to get a marked stimulation of breathing. This would seem to add some support to the idea of carbon dioxide primacy in the control of respiration in this age group. In their more recent work[11] they have demonstrated an important correlation between respiratory rate and general prognosis. The infants studied were divided into three groups. Group 1 had the best prognosis and were those who had a respiratory rate of about 40/min. immediately after birth and continued with that rate. They showed a progressively increasing resting tidal volume and were normal, well babies. Those in Group II had an initially high rate but came down to around 40 sometime between 6 hours and several days. They also had a progressive increase in resting tidal volume and their prognosis was good. The infants in Group III started out with a normal rate, but increased up to 60/min. within 36 hours. These infants did not respond with an increasing resting tidal volume and had to meet their respiratory needs with an increase in rate. This was associated with a reduction in resting tidal volume, severe uncompensated respiratory acidosis and occasional hypoxia. This group had the poorest prognosis.

From the foregoing, it can be seen that there is some difference in opinion as to the interpretation of the different respiratory patterns. Our studies indicate that the decision to use oxygen therapy or other medicinal stimulants should be made on the basis of a general appraisal of such factors as cyanosis, feeble heart action, shock, weak cry and lack of response to stimulants in addition to the type and efficiency of respiration. This is becoming a matter of some importance for evidence is accumulating rapidly to indicate that especially in premature infants toxic results of oxygen administration such as retrolental fibroplasia and pulmonary irritation occur from concentrations higher than 40 to 50%.

For many years Johnston[12] has been getting definite clinical improvement in bulbar polio patients with respiratory difficulty from the use of intravenous hypertonic glucose solution. He was anxious to see if we could show that improvement graphically by means of our respiratory tracings. We planned to make the study on actual polio cases, but since there were none in the hospital during that time it was done on unrelated cases. Tracings were made of the chest and abdominal movements on five children during the administration of 50cc of 25% glucose solution over a 5 minute period. The excitement incident to the venapuncture did cause some stimulation of respiration which had to be considered in the final analysis of the results. However, there was one case in whom a previous cut-down made it possible to give the solution without disturbance. Two of the five responded with a stimulation of respiration, two got a sedative effect and one showed no change. From these few cases, we concluded that the beneficial effects of hypertonic glucose given intravenously were not immediately interpretable in our tracings so far as any consistent pattern was concerned. However, there was a measurable change noted in 80% of the cases which was compatible with the clinical improvement observed, since an increased respiratory effort might be very helpful to one patient whereas a reduction in that effort could be the sign of improvement in another. A more definite trend might emerge from a larger series of cases.

While doing the plethysmograph studies on newborns, we wondered whether a study of the capillary blood flow as observed at the base of the finger or toe nail with a microscope would give information of value in conjunction with the former. There were many technical difficulties, as it was extremely important to get a sufficient fixation of the tiny finger or toe under the objective of the scope without constricting the normal flow. Even with several different plaster splints and a modern, powerful, dissecting microscope, the results were examination of the normal capillaries and did not add anything.

At present, we are working with a Woods' oxymeter. It is a fine precision instrument with which one can get a continuous measurement of oxygen saturation by means of a photoelectric cell attached to the ear. Papers have appeared on its use in newborns, and the results seem to be well worth while. Kennedy and his group[13] showed that oxygen saturation in the newborn averaged 67% at birth, and rose to an average of 89% in 17 minutes and 94% in 2 hours. Miller[14] used it in connection with his work on respiratory rate referred to above. He found that the infants in the more favorable groups had a consistently better oxygen saturation. This apparatus differs from those now in use in the Respiratory Center of this hospital, in that the

ear piece is very small and was designed especially for newborn infants. Also, the percent saturation is expressed as an absolute figure without the usual gasometric test on a blood sample to establish a base line. The accuracy is within 3% at 90% saturation and 9% at 50% saturation. These features make it extremely valuable for work on the newborn as the saturation can be followed right from birth on, with practically no disturbance to the infant. We are joining with Churchill and Lafontaine to show some correlation between his electro encephalogram and neurological examinations[15] and our respiratory studies and oxygen saturation. It is felt that such a program will add additional information on the etiology of some cases of cerebral palsy and mental deficiency.

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THE PHYSICIAN AND THE ADOPTION OF CHILDREN

ERNEST H. WATSON, M.D.*

Physicians in general practice or those specializing in pediatrics or obstetrics and gynecology are thought by many persons to be in a position to know where there are babies for adoption and to be in a position to exert considerable influence in behalf of one party or another. There is, of course, some truth in these suppositions but the physician is asking for trouble when he agrees to be the principal "go-between" in the matter of finding babies for childless couples or finding a new home for an unwanted baby. The physician may indeed jeopardize an adoption by failing to know and observe the cardinal principles which must underlie any successful adoption. These principles include a most important one, namely, the preservation of complete anonymity between the natural parent and the adoptive parent. This is best achieved by first having the natural parents give up all right to the child. This is a function for the probate court or a duly authorized agency. In most states it is against the law for a physician or a hospital to give "free" service and advice to a woman illegitimately pregnant on the condition that she release her baby for adoption to a certain couple. The physician should be aware of this and other laws pertaining to adoption if he is to enter in any way into this important transaction.

There is one point at which the physician may hinder adoptive practices, through thoughtlessness or failure to understand all the considerations when a child is to be placed in a new home. First and foremost in all such transactions should be the finding of a suitable home for the child. This consideration must take precedence over such problems as finding a child for a childless family or the solution of social problems of illegitimate pregnancies, payment of hospital bills or relief of county or community of the burden of caring for a homeless child.

Physicians are conditioned to respond when asked for help and it may be difficult to put the child's welfare first when childless couples who may be friends or patients appeal to the physician to help them find a child for adoption. Without considering the matter very deeply the physician may not realize that this particular couple are not good adoptive parents. Their desire for the child may be that of trying to hold together a shaky marriage, or to be in style in their social set, or to attempt to replace a recently lost child. When the trained social worker recognizes any of these motives as being paramount in the adoptive parents' feelings, he wisely puts them off. Our own state laws (Michigan) states that the Judge of Probate is required to have a full investigation "by the county agent, probation officer, or by a placement agency licensed by the state, or by the Michigan Children's Institute or the State Department of Social Welfare". The purpose of the investigation is to determine several things; the integrity, health and stability of the home into which it is proposed to place the child, the physical and mental health of the child, the child's family background and suitability of the child and adoptive parents on racial, religious and cultural backgrounds.

Almost every week one sees in the newspapers an account of a legal battle going on between natural parents who had previously released their child to a couple who

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have brought it up as their own and who may suddenly find themselves without any legal protection at all when the natural mother insists upon having her child back. It is virtually impossible to have this happen when well known rules of proper adoptive procedures have been observed. We have the recent example of the couple fleeing to Florida to escape the Massachusetts ruling that they would have to give up a child they thought theirs for six years, because the natural mother had discovered a difference in religious faith between herself and the adoptive parents. These tradegies cannot possibly be resolved satisfactorily. They should be prevented in the first place by having the adoption adequately safeguarded. Someone must remain heartbroken when final decisions are made in cases like this one.

The Child Welfare League of America has suggested the following set of minimum safeguards in adoption:

I. The safeguards that the child should be given are:

1. That he be not unnecessarily deprived of his kinship ties.
2. That the family asking for him have a good home and good family life to offer, and that the prospective parents be well adjusted to each other.
3. That he is wanted for the purpose of completing an otherwise incomplete family group in which he will be given support, education, loving care, and the feeling of security to which any child is entitled.

II. The safeguards that the adopting family should expect are:

1. That the identity of the adpoting parents should be kept from the natural parents.
2. That the child have the intelligence and the physical and metal background to meet the reasonable expections of the adoptive parents.
3. That the adoption proceedings be completed without unnecessary publicity.

III. The safeguards that the state should require for its own and the child's protection are:

1. That the adopting parents should realize, in taking the child for adoption, they assume as serious and permanent an obligation as do parents rearing their own children, including the right to inherit.
2. That there be a trial period of residence of reasonable length for the best interests of the family and the child, whether there be a legal requirement for it or not.
3. That the adoption procedure be flexible enough to avoid encouragement of illegitimacy on the one hand and trafficking in babies on the other.
4. That the birth records of an adopted child be so revised as to shield him from unnecessary embrassment in cases of illegitimacy.

Physician and Adoption of Children

The physician may play an important role in adoptive procedures and is on safe ground so long as he confines his efforts to giving medical advice. He is the only one who can give advice on matters of health, growth and development, and genetic influences relating to the infant, and on the natural mother's prenatal care. The details of the birth, and medical and developmental records on the infant are all extremely important factors in final decisions as to placement. Few, if any, human beings are perfect specimens. This applies to babies considered for adoption. Only a physician can advise on the probable long-term influence of such abnormal findings as the child may have.

Physicians should know the agencies in the community to which he can refer childless couples seeking infants, or natural parents who think they cannot take care of children (born or unborn). The physician is usually in a position to help the agency and to increase its effectiveness and prestige by his support.

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NEONATAL CHICKEN POX

E. O. JODAR, M.D.*

In a brief review of the literature only eleven cases of neonatal or intrauterine Chicken Pox could be found. Hubbard[1] in 1878 reported typical Vai-rcella in a one day old infant. In 1939 Shuman[2] reviewed the literature of 6 cases and reported a 7th. In 1939 Campbell[3] reported another case. In 1944 Oppenheimer[4] reported congenital Chicken Pox with visceral lesions. In 1947 Lucchesi, LaBocetta, and Peale[5] reported the 10th case and in 1948 Caravias Vera[6] reported the 11th. Other cases in which Chicken Pox was transmitted in utero have been reported in which the infant did not survive. The present case I believe worthy of being reported.

Case Report: On April 6, 1957 a 7 pound female infant was born to a mother who had encrusted lesions of Chicken Pox. The infant had a normal temperature of 99°F and appeared perfectly well except for skin lesions. Several clear vesicles were scattered over the body and there were also some crusts for a total of 8 lesions. A photograph taken one hour after birth showed typical "tear-drop" lesions.

Questioning the mother revealed that she had been exposed to a child with Chicken Pox in my office on March 9, 1957 and showed her initial lesion on March 23, 1957 which was 14 days later. She gave no other history of Chicken Pox and had no scars indicating previous disease.

Course: The infant was taken home at once and did not develop further lesions. She was never ill and within one week all scabs had disappeared. After one month several scars were present.

On April 9, 1957 the 15 month old male sibling showed his first lesion of Chicken Pox and the course of his illness was typical for a mild form of this disease. This child had been in my office on March 9, 1957 but apparently did not contract the disease at this exposure as did his mother.

Since this infant was immediately isolated at birth because the attending nurse thought the infant had Impetigo no other cases developed in the nursery. The mother was also isolated until removed from the hospital the next day and no new cases occurred among her contacts.

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*Department of Pediatrics, Visiting Staff.

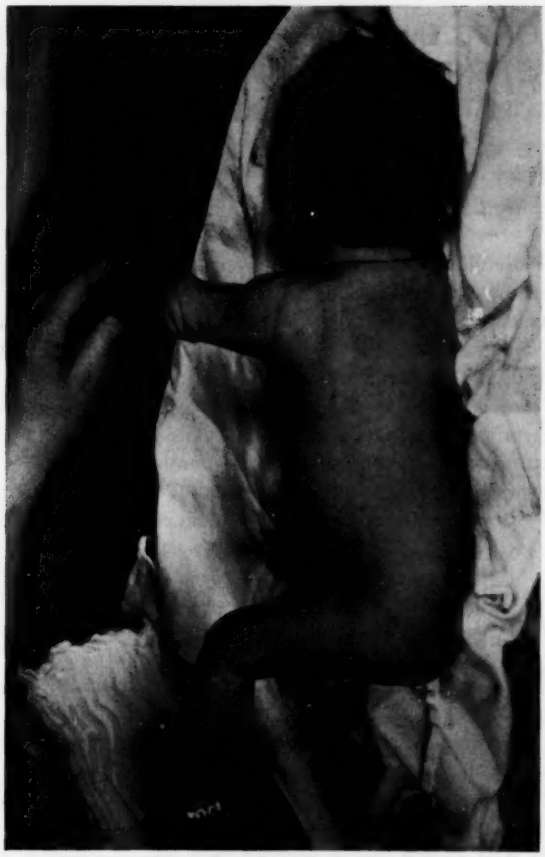

Figure 1. Infant with Chicken Pox, Age 1 hour.

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ABSTRACTS OF RECENT PUBLICATIONS OF THE PROFESSIONAL STAFF OF THE HENRY FORD HOSPITAL AND THE EDSEL B. FORD INSTITUTE FOR MEDICAL RESEARCH

***COMPARATIVE VALUE OF X-RAY DIFFRACTION AND INFRARED SPECTROPHOTOMETRY IN IDENTIFYING CERTAIN STEROLS AND THEIR DIGITONIDES.** W. T. Beher, J. Parsons, and G. D. Baker. Anal. Chem. 29:1147, 1957.

The relative usefulness of infrared spectrophotometry and x-ray powder diffraction methods for the identification of some biologically occurring sterols has been investigated. The data show that x-ray powder diffraction methods are superior to infrared spectrophotometry for the identification of sterols in the C_{27} to C_{29} series. On the other hand, neither method is capable of indentifying the sterol digitonides. Two hypotheses are proposed to explain the similarity of the absorption spectra of digitonin and sterol digitonides. Experimental evidence disclosed that the digitonin masks the characteristic absorption bands of the sterols. The use of x-ray diffraction definitely establishes sterol digitonides as chemical compounds, whereas infrared spectrophotometry does not distinguish between a simple mixture and a corresponding digitonide.

THE USE OF THE THREE-SECOND VITAL CAPACITY AND DIRECT TESTING OF BRONCHIAL ALLERGY. G. L. Brinkman and J. H. Burger. J. Allergy 28:346, 1957.

Direct bronchial testing of patients with clinical evidence of ragweed sensitivity was undertaken. The Vital Capacity and 3 second Vital Capacity were obtained prior to and following the inhalation of increasing strengths of an aerosol of ragweed antigen, with the following results:

Four patients with asthma and the skin test positive to ragweed were tested and all 4 gave a positive bronchial test.

Ten patients with asthma but a negative skin test to ragweed were tested and only one positive bronchial test obtained.

Three patients with vasomotor rhinitis and a positive skin test for ragweed were also studied and one positive bronchial test obtained.

Reduction in the 3 second Vital Capacity proved to be no more sensitive than reduction in the Total Vital Capacity. It was concluded that despite the known limitations of skin testing patients with asthma, direct bronchial testing gives insufficient additional information to justify it as a routine procedure.

THE USE OF ACTH AND CORTISONE IN TRICHINOSIS. G. L. Brinkman and L. Koos. J. Michigan M. Soc. 56:867, 1957.

Three cases of trichinosis in one family are reported. All three cases were treated by steroid therapy with dramatic and immediate symptomatic responses. Review of the world literature reveals that twenty-nine other cases of trichinosis treated with steroid therapy showed similar dramatic responses. There have been no fatalities amongst the cases so treated. The mode of action of these drugs is briefly reviewed

*From the Edsel B. Ford Institute for Medical Research.

and the reason for advocating maintenance of therapy for at least six weeks is given.

THE PROPHYLAXIS OF CARDIAC ARRHYTHMIAS COMPLICATING PULMONARY SURGERY. C. I. CERNEY. J. Thoracic Surg. 34:105, 1957.

Sixteen cases of cardiac arrhythmias occurring in the postoperative course of pulmonary lobectomy and pneumonectomy are presented. This represents an incidence of 29.4 per cent, following pneumonectomy, and 14.3 per cent, following lobectomy, or a combined incidence of 20.8 per cent following pulmonary surgery in 77 cases Possible etiological factors are discussed and because of the incidence, morbidity, and possible mortality, routine prophylaxis with quinidine and atropine is suggested. Since the majority of these patients can take oral medication immediately after surgery, the proposed schedule would be: (1) Quinidine 0.2 gm. four times daily, with an added 0.2 gm. of enteric-coated quinidine at bedtime, and (2) atropine 1 mg. four times daily (or other anticholinergic equivalent). Such medication should be started on the first postoperative day and continued through the thirtieth postoperative day. A constant expectant observation of the patient should be continued through the postoperative course and should arrhythmia occur, in spite of prophylaxis, rapid digitalization with Cedilanid or acetyl strophanthin should be instituted. If slowing does not occur, therapeutic doses of quinidine should be given without delay.

LUMBAR AND PERIPHERAL ARTERIOGRAPHY: TECHNICS AND RADIOLOGIC ANATOMY. W. R. EYLER. Radiology 69:165, 1957.

Lumbar aortography and demonstration of the distal branches of the aorta have become accepted and commonplace procedures. This presentation concerns primarily some of those aspects of the roentgen anatomy demonstrated by aortography and arteriography which are important in deciding upon and planning the surgical approach to the arteriosclerotic aorta and its lower branches. The material is drawn from a series of 600 aortograms and arteriograms. That an arteriosclerotic abdominal aneurysm is a lethal lesion has been well shown. Though the end-results of surgical replacement remain to be determined, there is now no doubt that a graft is frequently life-saving. Similarly, relief of intermittent claudication and the preservation of a limb that would otherwise be amputated are ample justification for surgical intervention in arterial insufficiency of the lower limbs. Arteriosclerotic aneurysms usually cause a lateral deviation and elevation of the aorta proximal to the aneurysm. This is of diagnostic and localizing value, particularly when the aneurysm shows only a narrow channel by aortography. The extent of segmental arterial disease is best shown by serial filming. The use of long serial films diminishes the amount of contrast material required. A single aortic injection can be used to demonstrate the vascular tree from the level of the renal arteries to the division of the popliteals. A simple device is described which facilitates serial filming with 14 x 36-inch cassettes.

THE BILLROTH I GASTRECTOMY. L. S. FALLIS. Surg., Gynec. & Obst. 105:107 1957.

Re-establishment of gastro-intestinal continuity after gastrectomy by direct anastomosis of the stomach to the duodenum was first carried out by Billroth in 1881. Since that time this procedure, known as the Billroth I gastrectomy, has had short periods of popularity alternating with long intervals of disinterest. The recent resurgence of favor that this operation has enjoyed lends an opportunity to again reassess

the value of the technique.

The operation is attractive from a physiologic and an anatomic point of view, but in the final analysis its merit must depend on proving that the end-results are better and that mortality and morbidity rates are not increased over those obtained with the Billroth II gastrectomy (gastrojejunostomy). There is some evidence to show that patients after Billroth I gastrectomy are more likely to regain or even surpass their normal weight level. Apart from this one feature there seems to be little to influence a choice between the two operations though the Billroth I is clearly indicated in re-operations for jejunal ulceration and as a measure to alleviate the dumping syndrome sometimes appearing after the Billroth II operation.

OBSERVATIONS ON INFESTATION BY SCHISTOSOMA MANSONI IN PUERTO RICAN TROOPS. W. S. HAUBRICH AND R. M. WELLS. U. S. Armed Forces M. J. 8:1093, 1957.

In a study of 43 young native Puerto Rican soldiers stationed in the continental U. S., slightly more than one third were found to harbor *Schistosoma mansoni* as manifested by ova in the stools (11 cases) or by granulomas in the rectal mucosa (11 cases) and liver (5 cases). Almost with exception the infestations were latent and asymptomatic. Active treatment of such disease by antimony potassium tartrate is attended by a high incidence of incapacitating side reactions, and its long-term value is debatable.

SEPSIS IN NORMAL AND PREMATURE INFANTS WITH LOCALIZATION IN THE HIP JOINT. P. J. HOWARD. Pediatrics 20:279, 1957.

The case reports of five patients with sepsis, localizing in the hip joint, are presented. The date of onset was before 30 days of age. The weights at birth were in the premature range in three, normal in two; the first clinical sign was swelling of the region of the hip and thigh. The organisms were coagulase positive staphylococci in three cases, unknown in two cases. The differential dignosis included cellulitis, trauma to the hip, and septic arthritis with abscess formation. Poliomyelitis, cancer, toxic synovitis and osteomyelitis of the femur were considered. Roentgenograms have been selected to show the slightness of the changes at onset, and the changes at 1, 5, and 12 years of age. Treatment should include general supportive measures, including administration of blood and nutritive elements, antibiotics and early drainage of the joint to prevent permanent damage of the head of the femur. This condition must be suspected in every instance of regional swelling of the hip in the newborn infant. Such swelling is an urgent indication for diagnostic aspiration of the joint.

LUMBAR AND PERIPHERAL ARTERIOGRAPHY. D. E. SZILAGYI. Radiology 69:177, 1957.

In surveying the more important vascular lesions in whose management lumbar and peripheral arteriography offers valuable assistance, the pathologic and clinical characteristics of occlusive and aneurysmal diseases of the aorta and its large branches have been briefly summarized. The essential role of arteriography in the rational planning of the surgical attack in occlusive arterial disease is stressed and the help to be gained from angiographic studies in the handling of aneurysmal disease is pointed

out. Brief mention has been made of some other peripheral arterial lesions in relation to which the applicability of arteriography must be kept in mind.

*STUDIES ON SUCCINIC DEHYDROGENASE V. ISOLATION AND PROPERTIES OF THE DEHYDROGENASE FROM BAKER'S YEAST. T. P. SINGER, V. MASSEY AND E. B. KEARNEY. Arch. of Biochem. & Biophysics 69:405, 1957.

1. The succinic dehydrogenase of baker's yeast has been solubilized and isolated from the particulate fraction of the cell wherein the enzyme is localized. The best preparations obtained were 65% pure by ultracentrifugal analysis.

2. The enzyme is an amber-brown protein, containing 4 atoms of iron and 1 mole of flavin per mole of protein. No method has been found to remove either the iron or the flavin without denaturation of the protein. The iron was readily liberated in the inorganic form by acid or thermal denaturation, but separation of the flavin form the protein required extensive proteolytic digestion of the latter. The flavin, set free in this manner, was not free FAD but, like that from the beef heart enzyme, appeared to be in bound forms, possibly as peptide derivatives.

3. The action of the enzyme is readily reversible. Inactivation on aging usually entailed a much greater loss of succinic dehydrogenase than of fumaric reductase activity, in accord with previous findings that the acceptors required in the former assay act by way of the iron while the electron donors used in the latter assay by-pass the iron and that aging alters the reactivity of enzyme-bound iron.

4. The following aspects of the action of the enzyme have been studied: effects of pH and temperature, specificity for electron carriers, inhibition by sulfhydryl reagents and iron complexors, kinetic constants for succinate, malonate, and fumarate, and turnover number.

5. In most respects the yeast enzyme resembles closely its counterpart in beef heart mitochondria.

RELATIONSHIPS OF CEREBRAL DISORDERS TO FAULTS IN DENTAL ENAMEL. W. F. VIA, JR. AND J. A. CHURCHILL. A.M.A.J. Dis. of Child. 94:137, 1957.

It is suspected that some of the abnormal processes causing damage to the brain might also produce defects in the enamel forming on the teeth at the same time. Hence a study was begun to determine the correlation between cerebral disorders and enamel hypoplasia. If a correlation exists, then the observed enamel faults in combination with suspected casual events from the medical history may allow a more accurate dating of the onset of the cerebral disorder.

Detailed information concerning heredity, gestation, birth and subsequent development was obtained from the parents or medical records of 100 children who had definite indications of cerebral dysfunction determined by clinical and laboratory means. The teeth of these children were examined and data concerning the location and type of enamel faults were tabulated. In addition 100 apparently normal children were examined for enamel faults. Those that had enamel defects were investigated to see if they had cerebral damage. The medical history of 40 of the normal children was investigated so that a comparison of possible etiological factors could be made.

The incidence of enamel hypoplasia among the normal group was 10%. In sharp contrast to this, 68% of the children in the cerebral damage group showed enamel

*From the Edsel B. Ford Institute for Medical Research.

hypoplasia. A comparison of the two groups revealed a Chi Square value of 58.84 indicating a P value considerably lower than 0.001. In the cerebral disorder group, 58 children had neonatal enamel hypoplasia and 19 children had prenatal enamel hypoplasia. Some children had both prenatal and neonatal hypoplasia. There was no prenatal hypoplasia noted in the normal group. The rate of enamel hypoplasia, neonatal, prenatal or both for each manifestation of cerebral disorder was found to be: Athetosis, 100% of 5 cases; spastic diplegia, 100% of 22 cases; hemiplegia, 43% of 14 cases; the epilepsies,, 54% of 22 cases; oligophrenia, 52% of 19 cases; combined disorders, 79% of 28 cases.

*MAGNETIC ALIGNMENT OF SINGLE IRON PARTICLES. JOHN H. L. WATSON. J. App. Physics, 28:821, 1957.

The orientation of single alpha iron particles under the effect of magnetic fields up to 25,000 gauss is described from electron micrographs of ultrathin sections cut from blocks of the particles which have been oriented in a liquid monomer and then "frozen" into position during polymerization. The micrographs demonstrate linear,. end-to-end attachment; circular, end-to-end attachment and streaming of particulate networks in the general direction of the aligning fields. The method has been developed to study directly the arrangement and distribution of elongated, fine particles of iron, freely suspended or packed and oriented in a liquid medium. It is useful for studying the extent and manner of heterogeneous particle packing, and of particle alignment under the influence of outside force fields.

Macroscopically the particles oriented easily but microscopic demonstration of alignment is difficult probably because the particles tend to minimize their magnetostatic energies rapidly and to form closed magnetic circuits. The method may provide a means of obtaining statistically quantitative estimates of the packing fraction and give direct observation of certain theoretical aspects of fine particle magnetism, particularly shape anisotropy.

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